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BAL (BRITISH ANTI-LEWISITE)*

Compiled by Dr. L. L. WATERS and Dr. CHESTER STOCK

IN a recent issue of *Nature,* Professor R. A. Peters of Oxford has announced the discovery and development during the war years of an effective antiarsenical, 2,3,-dimercaptopropanol.[1] This substance has been called BAL (British anti-lewisite). As its name suggests, BAL is of interest in war medicine as an effective therapeutic agent against both the local and systemic action of certain arsenical war gases. Clinical trials of BAL, conducted as a part of the program of war research, have shown further that the compound is of value in the treatment of types of arsenical poisoning encountered in civilian medicine. Beyond this direct clinical application, the study of the action of BAL has resulted, as stressed by Professor Peters, in an important advance in the understanding of fundamental biochemical mechanisms.

Full details concerning BAL, its chemistry, method of preparation and basic biochemical actions were promptly and graciously transmitted to the United States by Professor Peters and his associates through official channels. BAL itself was received in this country late in 1941. Thereafter an intense program of study, including preparation and manufacture, biochemistry, toxicology, pharmacology, experimental therapeutics and clinical application, was undertaken jointly by the Government agencies concerned. Cooperating in this program were the U. S. Army, the U. S. Navy, the Office of Scientific Research and Development, the National Research Council, the Federal Security Agency.

It is the purpose of this review to give a brief summary of the information on BAL, particularly as it was developed in the United States. As in England, more detailed papers based on the original confidential reports are being prepared for early publication.

* Many of the investigations included in the footnotes have not been published in open literature and the date given is the year in which the work was carried out.

[1] R. A. Peters, *Nature,* November 24, 1945.

Preparation and Chemistry

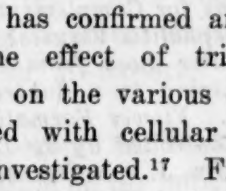
Subsequent to the discovery of BAL by the British, methods of preparation of BAL were studied in the United States so that a process would be available for large-scale manufacture.[2] A modification of the British process was developed involving the bromination of allyl alcohol to glycerol dibromohydrin (83 per cent. yield) followed by reaction in an autoclave with sodium hydrosulfide under 100 pounds per square inch hydrogen sulfide pressure, at 60–70° C. to yield BAL (64 per cent. yield). BAL is unstable to heat and to acids and decomposes during distillation. The British and American investigators independently made the important discovery that 1 per cent. of ammonium hydroxide is an efficient stabilizer during vacuum distillation.

Other methods, as well as many modifications of the above method and a variety of reaction conditions, were studied before developing a process which was operable and which yielded a product of satisfactory quality. On the basis of biological tests BAL produced by the recommended procedure was equal to that produced by the British. This process was expanded to pilot plant scale operation.[3] The pilot plant yields were about the same as indicated above. This pilot plant produced the BAL used by the Services in the form of therapeutic solutions and ointments. An engineering study[4] was also made of a plant capable of producing 200,000 pounds of BAL per year; at that time it seemed possible that there would be a large demand for this material.

Other work on the chemistry of BAL confirmed the demonstration by the British that this and other dithiols form with lewisite and lewisite oxide isolable cyclic dithioarsenites.[5] Further work was conducted on the resolution of BAL into its optically active forms.[6] Investigations[7, 8] were also carried out on the preparation of a considerable number of water-soluble derivatives of BAL and on a large number of analogs.

Biochemical Action

Peters and his associates[1] found that sodium arsenite and lewisite exerted a powerful inhibitory influence on the pyruvate oxidase system in brain brei, a system dependent upon –SH groups for its activity. They next analyzed compounds of arsenic with an –SH protein product, kerateine. The arsenic content of the arsenic-kerateine compound was found to correspond closely with the thiol content of the parent protein. Further, most of the arsenic present in the treated protein was in combination with two thiol groups. This and other chemical evidence indicated that dithiols added to protein previously treated with arsenic probably compete successfully for the arsenic by the formation of compounds of the type:



These findings focused attention on the theory for which there was already considerable independent evidence[9, 10, 11, 12, 13, 14, 15, 16] that the toxicity of trivalent arsenicals is largely due to their binding of essential thiol groups in enzyme proteins. This concept was supported by the significant observation that dithiols of the BAL type not only prevented the inhibition of enzyme systems by arsenicals but also reactivated these systems when added after inhibition had occurred.[1]

American work has confirmed and extended these observations. The effect of trivalent arsenicals, chiefly of lewisite, on the various classes of enzyme reactions concerned with cellular metabolism have been intensively investigated.[17] From these experiments it is concluded that trivalent arsenicals exert their toxic action by combination with –SH groups of the activating protein of enzyme systems. Tissue respiration is interfered with by the action of the arsenicals on the large group of –SH enzymes essential for carbohydrate transformations and fat metabolism. Lewisite has little effect on co-enzymes or on enzyme systems concerned with protein utilization and synthesis. The enzyme inhibitions produced by lewisite and arsenic can generally be prevented by BAL or other closely related dithiols. Furthermore, even when established, these inhibitions can be reversed by BAL and to a lesser extent by glutathione. Certain of the inhibitions produced by arsine are enhanced by BAL.[18] This is apparently

[2] P. L. Salzberg, W. A. Lazier, M. W. Farlow, W. J. Peppel, G. W. Rigby, F. K. Signaigo, C. G. Wortz, 1942.
[3] H. W. Elley, W. S. Calcott, H. R. Lee, C. F. Belcher, A. J. Wuertz, 1942.
[4] H. W. Elley, C. B. Biswell, J. F. Froning, W. V. Wirth, T. W. Stricklin, Jr., 1943.
[5] P. D. Bartlett, S. G. Cohen, H. J. Dauben, Jr., L. J. Rosen, M. J. Ryan, 1942.
[6] H. R. Snyder, R. L. Kenyon, 1943.
[7] P. L. Salzberg, W. A. Lazier, F. K. Signaigo, A. A. Pavlic, 1945.
[8] M. S. Kharasch, S. Weinhouse, 1943.
[9] M. Onaka, *z. physiol. chem.*, 70: 433–440, 1911.
[10] A. Szent-Györgyi, *Biochem. Jour.*, 24: 1723–1727, 1930.
[11] C. Voegtlin, S. M. Rosenthal, J. M. Johnson, *U. S. Pub. Health Report*, 46: 339–354, 1931.
[12] C. Voegtlin, H. Dyer, C. S. Leonard, *U. S. Pub. Health Report*, 38: 1882–1912, 1923.
[13] R. Labes, *Arch. Exp. Path. Pharmakol.*, 141: 148–160, 1928.
[14] M. S. Kharasch, U. S. Patent 1927, 1, 677, 392.
[15] H. J Barber, *Chemistry and Ind.*, 49: 802, 1930.
[16] A. Cohen, H. King, W. I. Strangeways, *Jour. Chem. Soc.*, 3043, 1931.
[17] E. S. G. Barron, Z. B. Miller, G. Bartlett, J. Meyer, 1942.
[18] C. J. Kensler, C. P. Rhoads, H. Levy, H. B. Sherlock, C. Brooks, 1943.

related to an inherent toxicity of BAL itself for the enzyme system in question. In reversing enzyme inhibitions produced by arsenic, BAL and other related dithiols exhibit greater affinity for arsenic than do the attacked tissue thiols. This is strikingly brought out in experiments on unicellular organisms.[19, 20] If trypanosomes or spermatozoa are subjected to lethal concentrations of arsenic and observed microscopically they lose all motility and show early degenerative changes. If a dithiol of the BAL type is now added they regain their motility and normal cytologic appearance.[19, 20] Apparently the arsenic is actually removed from the damaged cells as the arsenic content of the supernatant fluid increases after the addition of BAL.[19] Experiments have also shown that the administration of BAL to animals previously poisoned with arsenicals is followed by a marked increase of arsenic excretion in the urine.[1, 19] Except in arsine poisoning no dithiol has been found which is more effective than BAL in preventing and reversing the toxic effects of the arsenicals tested.[18]

BAL is a strong reducing agent and is rapidly oxidized in the presence of catalytic amounts of copper and hemin. In the presence of oxygen, it destroys hemin or oxyhemoglobin by opening the porphyrin ring. BAL reacts instantaneously with methemoglobin and reduces it to hemoglobin. Cytochrome C is kept in a reduced state by BAL and thus interference with cytochrome oxidase activity is produced. BAL exerts an inhibitory effect on brain glycolysis presumably by combining with the metal-protein components which take part in the enzymatic processes concerned. Oxidized BAL itself is an inhibitor of enzyme systems containing essential –SH groups. It also destroys the physiological activity of insulin, possibly by reduction of the –S–S– groups of the insulin molecule. These reactions of BAL[21] may be related to the toxicity of the compound when injected in large amounts.

Working with the –SH containing enzyme, succinoxidase, it has been shown that heavy metals such as Pb, Sb, V, Bi, Cd, Hg and Zn produce complete inhibition and that the enzyme is reactivated on the addition of certain BAL derivatives. This demonstrates that the toxicity of these metals is, like that of As, due to inhibition of –SH enzymes. It furthermore is an indication for experiments designed to test the therapeutic value of BAL in these heavy metal intoxications.[22]

Toxicology and Pharmacology

BAL is not an innocuous substance. With its initial use, Peters and his associates[1] observed profound toxic effects following its administration to rats. When death occurred in these animals, it was usually preceded by violent convulsive seizures. Following the administration of toxic amounts of BAL to laboratory animals, there is usually an initial period of apathy, accompanied by lacrimation, blepharospasm and edema of the conjunctivae. There is copious salivation, and dogs frequently vomit. If the dose is increased, the course is further characterized by an increase in depth and rate of respiration, by muscle tremors of gradually increasing intensity, a rapid, thready pulse, nystagmus, and finally by repeated tonic and clonic convulsions, coma and death.[23, 24, 25]

Lethal amounts of BAL given intramuscularly or percutaneously cause an early transient rise in blood pressure which results from intense vasoconstriction in skin and skeletal muscle.[24] Rapid intravenous injection of large doses of BAL is followed by circulatory collapse. Changes in the electrocardiogram and the cardiac arrest occurring in hearts perfused with BAL solutions give additional evidence of the toxicity of BAL for the heart.

Following the injection of toxic amounts of BAL, the pH of the blood is reduced, as are also the serum CO_2 content and combining power[23, 24] Accumulation of lactic acid and a fall in serum sodium contribute to the metabolic acidosis.[23] Terminally there is a rise in serum amino acids, hyperglycemia, a depletion of liver glycogen and a virtual depletion of intracellular hepatic potassium.[23] The glycogen content of skeletal or cardiac muscle is not materially affected.[24]

The striking physiologic and metabolic changes of BAL poisoning in animals are not accompanied by comparable morphologic alterations. Little is to be seen either grossly or microscopically other than congestion of the viscera, and occasionally accumulation of fluid in the serous cavities or lungs.[23, 24] Lesions of the central nervous system have been described following the injection of certain BAL derivatives.[24]

On the skin of man or animals, BAL causes localized erythema and edema but no necrosis or blister formation. BAL is extremely irritating when applied to mucous surfaces, producing edema and severe ulcerations of the respiratory passages[17] and gastric mucosa of animals.[24] Fortunately, dilutions still therapeutically active, on the order of 5–10 per cent., may be applied to the eye or injected intramuscularly with no lasting ill effects. In man, solutions

[19] H. Eagle, 1942–1943.
[20] J. McLeod, 1942.
[21] E. S. G. Barron, Z. B. Miller, T. P. Singer, J. Meyer, 1943.
[22] E. S. G. Barron, S. Kalnitsky, 1944.
[23] H. Bunting, W. Ordway, H. Harrison, S. Durlacher, W. S. Albrink, 1942, 1943.
[24] McK. Cattell, H. Gold, W. Modell, M. B. Chenoweth, S. Krop, P. Hitchcock, F. Foster, W. F. Riker, 1942–1943.
[25] R. W. Gerard, J. Tobias, A. Potts, C. Lushbaugh, F. Simon, H. Patt, M. Swift, S. Postel, L. Postelnek, 1944.

or ointments containing 5–10 per cent. BAL produce only temporary tearing, lacrimation, blepharospasm and eye pain when instilled into the conjunctival sac.[26, 27, 28, 35, 36] Injected intramuscularly in sterile peanut oil-benzyl benzoate solution, concentrations of BAL of 10 per cent. or less are well tolerated.[29, 30, 31, 34] Inunction of a total of 1 cc of undiluted BAL or of 2 gm in a jelly base does not produce systemic effects in man.[31, 32]

It has been shown that BAL-in-oil injected intramuscularly at a dosage level of 3 mgm per kg produces only the mildest reactions in a small percentage of the individuals tested.[29] If, however, the level is increased to 5 mgm per kg, more than half the subjects experience some or all of the following reactions: nausea, vomiting, headaches, generalized aches and pains, burning sensations in the mouth, nose and eyes, sweating, restlessness, weakness, pain in the limbs, jaws and trunk muscles. The heart rate is often increased and there may be a rise in both systolic and diastolic blood pressure.[29, 30, 31] These signs and symptoms are transient and subside within four hours.

The early samples of BAL produced in the United States by the hydrogenation of the appropriate polysulfides were much more toxic than the BAL received from England.[23] Subsequent syntheses by the modified British procedure yielded a BAL which in toxicity and therapeutic efficacy was comparable to the British samples.[2, 23, 34] This product was eventually established as American Reference Standard BAL,[33, 34] and its physical, chemical and pharmacological properties have served as standards for the control testing of all BAL produced in the United States.[34] The LD_{50} of American Reference Standard BAL for rats is 105 mgm per kg when injected intramuscularly.

Experimental Therapeutics

Beginning in the spring of 1942 a large number of animal experiments were carried out in order to test the therapeutic value of BAL against the arsenicals used in chemical warfare. Most of the experiments were concerned with combatting the local effects of these chemical agents on the eyes and skin. While chiefly of interest to war medicine, the therapeutic results achieved were so striking that they deserve brief mention. It was found, in agreement with British reports,[1] that following the contamination of rabbits' eyes with an amount of lewisite sufficient to destroy the eyes, the local instillation of 5 or 10 per cent. solution of BAL up to 5 minutes after contamination resulted in almost complete recovery.[35, 36] At time intervals longer than five minutes, treatment resulted in progressively less good results, but some improvement was observed even after a treatment delay of thirty minutes.[35, 36]

The effect of BAL on the lesions produced by lewisite and other vesicant arsenicals on the skin of animals was equally striking.[1, 37, 38] Prompt application of solutions or ointment containing the medication prevented these lesions completely.[37, 38] Even after initial erythema had appeared, applications of BAL prevented the further development of the process and were followed by the rapid disappearance of the initial redness.[37, 38]

Accidental contamination of human eyes with lewisite occurred only rarely during the war, so that direct observations on the efficacy of BAL were few. The instances reported would seem to support the results obtained in animals.[39] The use of volunteers made possible extensive therapeutic trials of BAL against the lesions produced by arsenicals on human skin. In such volunteers the material proved just as effective in preventing the development of vesicant lesions after the application of lewisite as it had in animals.[32, 40, 41]

Once the therapeutic value of BAL had been established for arsenical lesions of eye and skin, and its toxicity in these locations had been determined, there remained the problems of the best possible vehicles for BAL, and proper packaging. Cooperative efforts involving much chemical and biological testing by Service and civilian government agencies and by manufacturers culminated in satisfactory issues for the Armed Forces of BAL eye solution,[34, 35, 36, 44, 45] BAL eye ointment[3, 34, 42, 43, 44, 45] and BAL ointment for skin application.[3, 43, 44, 45]

Lewisite and other arsenicals when applied to the skin of animals in sufficient quantity are absorbed

[26] C. P. Rhoads, A. S. Reese, 1942.
[27] M. B. Sulzberger, M. Cuthbert, D. P. Barr, J. McLean, 1943–1944.
[28] R. C. Laughlin, 1944.
[29] H. Eagle, H. J. Magnuson, R. Fleishman, 1943–1944.
[30] H. Gold, W. Modell, McK. Cattell, 1944.
[31] M. B. Sulzberger, R. L. Baer, A. Kanof, 1944.
[32] D. W. Wilson, T. R. Talbot, 1943–1944.
[33] P. L. Salzberg, W. A. Lazier, G. W. Rigby, C. G. Wortz, 1943–1944.
[34] H. O. Calvery, H. A. Braun, D. W. Fassett, O. G. Fitzhugh, C. D. Johnston, W. S. Lawrence, L. M. Lusky, A. A. Nelson, R. B. Smith, Jr., B. J. Vos, Jr., G. Woodard, 1943–1944.
[35] F. H. Adler, I. H. Leopold, A. S. Crandall, W. H. Steele, 1942.
[36] W. F. Hughes, Jr., 1942.
[37] C. B. Marquand, O. E. McElroy, T. W. Kethley, 1941.
[38] M. B. Sulzberger, D. P. Barr, 1942.
[39] Medical Division, Chemical Warfare Service.
[40] D. P. Barr, M. B. Sulzberger, 1942.
[41] W. Bloom, T. Friedman, J. Last, R. Murray, J. Savit, 1942.
[42] J. S. Friedenwald, 1942.
[43] M. B. Sulzberger, D. P. Barr, J. McLean, R. L. Baer, M. Cuthbert, C. Lowenberg, 1943.
[44] P. L. Salzberg, W. A. Lazier, M. W. Farlow, G. W. Rigby, C. G. Wortz, 1943.
[45] P. L. Salzberg, W. A. Lazier, G. W. Rigby, C. G. Wortz, 1945.

and cause systemic arsenic poisoning. The effectiveness of BAL in protecting such contaminated animals from the systemic action of lewisite was early observed by the British investigators.[1] Treatment not only saved the animals but also resulted in increased urinary excretion of arsenic.[1] Work in the United States has abundantly confirmed these observations[19, 23, 29, 46] and has indicated that to obtain this protective action against systemic effects BAL need not be applied directly to the site of lewisite contamination.[23]

As mentioned earlier, BAL was capable of resuscitating microorganisms poisoned by various trivalent arsenicals, including the widely used antisyphilitic agent mapharsen.[19, 20] BAL given intravenously, intramuscularly or subcutaneously also resuscitated rabbits[19] or cats[24] given lethal injections of mapharsen. The longer the delay in treatment after injection of the arsenical, the less effective BAL became in preventing systemic effects. Urinary excretion of arsenic was greatly increased following treatment with BAL. Furthermore, subcutaneous, intramuscular or intravenous administration of BAL prevented the development of systemic arsenical poisoning due to lewisite or phenyldichlorarsine.[19, 29, 47] Application of BAL to lewisite-burned areas combined with parenteral injections was ultimately found to be the most effective method of therapy.[47]

These experiments led directly to further studies in animals of the toxicity and therapeutic effectiveness of BAL in various vehicles, by various routes of administration and on various dosage schedules.[19] The data so obtained made possible the development of a stable sterile preparation of BAL in benzyl benzoate-peanut oil solution, suitable for intramuscular injection.[19] The most effective method of treatment was found to consist of four injections of BAL at two to four hourly intervals, followed by single daily injections for six days.[19] On this schedule, BAL in doses of 1 to 10 mg per kg per injection saved 55 per cent. of the animals from repeated massive doses of mapharsen and delayed death in an additional 22 per cent. Similar results were obtained in the treatment of animals poisoned with lewisite, applied either to the skin,[23] or subcutaneously,[29] and treated with the BAL peanut oil-benzyl benzoate preparation.

The toxicity of this preparation on intramuscular injection in man was then carefully investigated.[29, 30, 31] When it was found that BAL could be injected safely into man in amounts that were therapeutically effective against arsenical poisoning in animals, it remained only to give BAL a therapeutic trial in instances of clinical arsenical poisoning.

There is now evidence from animal experiments that BAL is of value in preventing the development of pulmonary lesions after the inhalation of lewisite,[23, 47] cadmium[25, 47] or zinc fumes.[48] It is also therapeutically active against systemic toxic actions of mercury[49] and possibly zinc. With cadmium, BAL forms toxic complexes in the body that cause serious renal damage although the animal is protected from the systemic action of cadmium itself.[50]

Medical Applications

Toxic reactions in man due to the systemic action of arsenic are observed occasionally during the arsenotherapy of syphilis. Because of the recent widespread use of highly intensive schedules of anti-syphilitic treatment the incidence of such reactions had increased markedly prior to the introduction of penicillin.[51] It thus became feasible to initiate a carefully supervised therapeutic trial of BAL in clinics where patients were being given these intensified forms of treatment.[29] Patients were also available from industrial plants where exposure to arsenicals had accidentally occurred.[52] Up to the present time more than 200 such patients have been studied in the United States and England.[1, 29] The majority of toxic reactions treated have been either arsenical dermatitis or hemorrhagic encephalitis, following administration of mapharsen. Included, however, are some cases of massive overdose of arsenicals and other less common manifestations of arsenic poisoning. Since the majority of the patients observed received conventional supportive therapy and supplementary medication, an exact assessment of the value of BAL was difficult. Also, customary caution with a new and toxic drug limited its use to patients so seriously ill as to endanger life. In spite of the difficulties thus introduced the available data strongly suggest that BAL properly administered is in fact effective in the treatment of patients with arsenical dermatitis, arsenical encephalitis and individuals who have received a massive overdose of mapharsen.[29, 52]

It is probably of value in some cases of blood dyscrasia resulting from arseno-therapy, and it appears to be of no value in most cases of so-called arsenical jaundice.[51]

In addition to its use in systemic arsenical poisoning, BAL has been given preliminary clinical trial in

[46] McK. Cattell, W. F. Riker, G. Rosenfeld, 1944.
[47] H. E. Harrison, S. H. Durlacher, W. S. Albrink, N. K. Ordway, H. Bunting, L. L. Waters, 1943–1944.
[48] A. Gilman, B. P. McNamara, 1943–1944.
[49] A. Gilman, R. Allen, F. S. Philips, 1944–1945.
[50] A. Gilman, R. Allen, F. S. Philips, 1943–1945.
[51] H. Eagle, R. B. Hogan, *Venereal Disease Information*, 24: 33, 1943.
[52] W. T. Longcope, M. M. Wintrobe, J. A. Leutscher, Jr., B. V. Jager, 1943.

mercury poisoning. As was anticipated from preceding animal experiments,[49] the results in these patients are most encouraging.[53]

In conclusion, it should be restated that BAL, discovered in England early in the war, has been developed through the joint effort of many agencies and individuals in Britain and in the United States as a therapeutic agent in local and systemic arsenical poisoning. Further, study of its mode of action has led to definite advances in biochemical theory. Necessary data for the consideration of BAL under the new provisions of the Federal Food, Drug and Cosmetic Act have been submitted to the Administrator of the Federal Security Agency. Although the substance itself and the large body of detailed reports on which this summary is based are not yet generally available, as soon as possible full information on BAL will be submitted to the Council on Pharmacy and Chemistry of the American Medical Association.

The above summary was compiled by L. L. Waters and C. Chester Stock for the following agencies:

1. Medical Division, Chemical Warfare Service, *and* Medical Department, Office of the Surgeon General, *U. S. Army.*
2. Bureau of Medicine and Surgery, *U. S. Navy.*
3. Division 5, Committee on Medical Research, and Division 9, National Defense Research Committee, *Office of Scientific Research and Development.*
4. The Committee on Treatment of Gas Casualties, Division of Medical Sciences, *National Research Council.*
5. Division of Pharmacology, Food and Drug Administration, *and* Venereal Disease Research Laboratory, U. S. Public Health Service, *Federal Security Agency.*

WASHINGTON, D. C.

OBITUARY

RICHARD STANISLAUS McCAFFERY

RICHARD STANISLAUS MCCAFFERY, respected professor of mining and metallurgy at the University of Wisconsin for twenty-seven years, died at his home in New York City on June 12, 1945, in his seventy-first year.

He was born in New York City on June 2, 1874, the only son of Michael and Mary McCaffery. He completed not only his elementary education in New York but also his professional studies at Columbia University, from which institution, in 1896, he received the degree of engineer of mines. In his senior year at Columbia he served as research assistant to Professor Henry M. Howe, one of the foremost metallurgists of that time, who instilled in him the desire for research.

From the time of his graduation in 1896 until 1909 he worked as a mining and metallurgical engineer in various places in South America and in New Mexico and Utah. Before leaving New York for his first assignment in Chile he was married to Kathleen Kirwan, of New York City, on January 27, 1897. Their honeymoon consisted of the trip to Chile to a rough and inaccessible mining camp. He often related to his students how the experience in Chile taught him to be self-reliant and how best to use the materials at hand. Upon his return to the United States in 1900, he became superintendent for the Santa Fe Gold and Copper Mining Company at San Pedro, New Mexico. From 1905 to 1907 he served as manager of the Salt Lake Copper Company at Salt Lake City, Utah, and from 1908 to 1909 he was superintendent for the Tintic Smelting Company at Silver City, Utah.

His teaching career was begun in 1909 as professor of mining and metallurgy at the University of Idaho. Here he remained for five years. Because of his previous professional experiences, he was asked to serve as consultant for many important lead and zinc mining companies in Idaho and he became an authority on the mineral deposits of that state.

In 1914 he joined the faculty of the College of Engineering of this university as professor of mining and metallurgy, and from 1915, for twenty-six years, he served as chairman of his department.

A few years before his retirement from active service, in 1941, his health began to fail. He then moved to New York City, where he and his wife could be near their children. Here he accepted such consulting activities as his failing health permitted. He is survived by his wife, four sons, Richard, Jr., Arthur L., Philip, John K., two daughters, Marian and Agatha (Mrs. Richard Church), and one sister, Nora McCaffery.

As a member of the faculty of this university, his greatest achievement was the development of the young student; his love and interest in them was boundless; he lived with them in his classes; he made it a practice to have them in his home; and he knew them so intimately he called them by their first names. To the student, on the other hand, he was affectionately known as "Mac." His kindly and sympathetic nature lives in the recollections of his students and associates who profited from his friendly advice. It has been truly said by one of his former pupils that he had the rare ability and the rare gift to make the most complicated and difficult problems appear simple and easily understood.

Professor McCaffery was a devout Catholic. He inaugurated discussion groups and was the leader in expounding the Catholic philosophy; and for many years he was a trustee of St. Paul's Catholic University Chapel.

[53] W. T. Longcope, J. A. Luetscher, Jr., 1945.

Professor McCaffery read widely in scientific publications. Furthermore, he maintained memberships in numerous scientific societies: American Association for the Advancement of Science, American Institute of Mining and Metallurgical Engineers, particularly its Committee on Iron and Steel, American Chemical Society, American Foundrymen's Association, American Society of Metals, Canadian Iron and Steel Institute, Institution of Metals and the New York Academy of Sciences.

Thus he kept abreast with the latest advances in the sciences and particularly in the science of metallurgy. He translated many technical articles in French and German publications. From these he often gained ideas for his own researches which contributed to advances in scientific methods for making iron and steel.

Among the best known of his researches are those on the viscosity and the constitution of blast furnace slags. These studies, extending over several years, appeared in the Proceedings of the American Institute of Mining and Metallurgical Engineers and the American Iron and Steel Institute. The information disclosed by these studies has been adopted as standard practice in the industry. He also obtained a patent on a basic lining for the bottom of a Bessemer converter.

In 1924 he promoted the idea of bringing instruction to students steadily employed in industry. The first off-campus instruction by the University of Wisconsin at the graduate level leading to a degree was given in Milwaukee. This off-campus graduate work in metallurgy inaugurated by Professor McCaffery has been continued.

In the passing of Professor McCaffery the university and the metallurgical industry have lost an able student, a resourceful investigator and an inspiring teacher.

Committee,
G. J. BARKER, *Chairman*
O. L. KOWALKE
M. O. WITHEY

UNIVERSITY OF WISCONSIN

DEATHS AND MEMORIALS

DR. THOMAS HUNT MORGAN, professor emeritus of biology of the California Institute of Technology, died on December 4 at the age of seventy-nine years.

CARL PURDY, student and cultivator of West American Liliaceae, died at Ukiah, Calif., on August 8. His most important paper, "A Revision of the Genus Calochortus," was published in the Proceedings of the California Academy of Sciences in 1901, but he also sent articles on Coast Range native plants to Charles Sprague Sargent's weekly, *Garden and Forest,* and to other periodicals. Born on March 16, 1861, at Danville, Mich., he went to California in 1870.

UNDER a resolution of the Senate Judiciary Committee the House of Representatives on December 3 approved a resolution designating January 5 as George Washington Carver Day.

IN commemoration of the centennial of the birth of William Conrad Roentgen and of the semi-centennial of his discovery of x-rays, a special exhibit of material relating to radiology was prepared for the Medical Branch Library in Galveston of the University of Texas. The exhibit included pioneer publications by Roentgen, the Curies and others, demonstrating the exploitation of radiant energy in medicine and indicating the relation of Roentgen's discoveries to the knowledge of atomic energy.

SCIENTIFIC EVENTS

RESOLUTIONS OF THE SOUTHWESTERN SECTION OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE

THE following resolutions signed by Chauncey D. Leake, *Chairman,* and Donald Slaughter, *Secretary,* have been passed by the Southwestern Society for Experimental Biology and Medicine:

WHEREAS, experimentation with animals under satisfactorily controlled conditions is necessary for the advancement of knowledge regarding living things, and

WHEREAS, such knowledge contributes enormously to the health and happiness of people everywhere, and

WHEREAS, such experimentation is continually subject to the threat of legislative interference, now be it

Resolved by the Southwestern Section of the Society for Experimental Biology and Medicine that respectful request be made to proper state and national legislative bodies, through the appropriate committees thereof, to assure the freedom of responsible scientific research in biology and medicine involving animal experiments, providing always that the animals in question are properly cared for and required to suffer no pain.

This resolution after discussion was carried unanimously.

WHEREAS, there is now much discussion regarding Federal subsidy in support of scientific endeavor, in order to assure the continuance of the benefits of scientific effort, and

WHEREAS, the many reports, published discussions, and other comments relating to this important matter do not

fully emphasize assurance of desired and continual freedom for scientific workers, now be it

Resolved by the Southwestern Section of the Society for Experimental Biology and Medicine that appropriate protagonists for Federal support of scientific work be informed of the Section's wish, in company with responsible scientists throughout the nation, to have clear assurance of freedom of scientific endeavor, under any form of Federal subsidy, support, or encouragement, with the understanding that such freedom extend not only to scientific studies and scientific undertakings themselves, but also to the reporting and discussion of results derived therefrom, and be it further

Resolved that the section express its concern lest any interference with the necessary freedom of scientific work and the reporting of data therefrom may result in the development of a scientific orthodoxy, which would be detrimental to the ideals of science and democracy and to the further development of our civilization.

This resolution after discussion was carried unanimously.

THE PHILADELPHIA RESOLUTION

MORE than twelve hundred scientists in the Philadelphia area, including the heads of university science departments and leaders in industrial laboratories, have gone on record (1) calling for a world authority to control the atomic bomb as a weapon, and (2) protesting the restrictive character of the May-Johnson Bill for the domestic control of atomic energy.

Later, at a meeting attended by more than 100 of these scientists, the following resolution, similar to that recommended by the Federation of Atomic Scientists, was unanimously adopted. It was also urged, in view of the importance of immediate action, that this resolution be given the widest possible publicity.

We Philadelphia scientists, aware of the tremendous import of atomic energy and atomic weapons to all mankind, believe that the security of the United States can be achieved only through the international cooperation for the joint control of these new forces. We believe that a policy of secret research and exclusive national control can only result in a ruinous competitive armaments race in which all the nations of the world will join, leading to the danger of a new and catastrophic world war. From such a war no people will emerge free, if indeed they survive at all.

We therefore resolve and urge:

1—That the United States as the country that has opened the way for the development of atomic energy, should immediately invite the governments of Great Britain and the Soviet Union to a conference to prevent competitive armaments and consider the problems arising from this overwhelming development.

2—That the United States champion the need for the international development with the broadest utilization of all resources and interchange of ideas.

We believe furthermore that any legislative effort which stifles free and open scientific investigation, which seeks to prevent public surveillance and criticism of the application of atomic energy, will stifle scientific progress, undermine peace and is therefore harmful to the national interest.

We therefore urge the Congress:

1—That legislative action for the control of atomic energy be preceded by full, free and public discussion.

2—That the authority for the guidance of the development of atomic energy shall consist of men of scientific competence, fully compensated for their services and able to work towards the maximum utilization of atomic energy for the welfare of the public and not for the interests of any special group.

3—That the administration chosen to direct the work of such an authority be a civilian. That the security regulations be limited to direct military application of atomic power and that free research and right of publication be immediately resumed in the field of atomic physics.

4—That radioactive and isotopic material and all scientific techniques and equipment be made immediately available to scientists. All purely scientific information, including patents, should be made available immediately.

THE ASSOCIATION OF LOS ALAMOS SCIENTISTS

THERE has been formed at the Manhattan District laboratory at Los Alamos, New Mexico, an association of the investigators working on the atomic bomb, called temporarily the Association of Los Alamos Scientists. The object of this organization is to promote attainment and use of scientific and technological advances in the best interests of humanity. The members of the organization recognize that investigators, by virtue of their special knowledge, have, in certain spheres, special political and social responsibilities beyond their obligations as individual citizens. The organization aims to help to carry out these responsibilities by keeping its members informed on current issues, and by the release of authoritative public statements on scientific questions in their relation to society.

The membership includes a large majority of the scientific workers at Los Alamos and, though at present limited to members of the laboratory staff, it is intended that this restriction shall be removed as soon as possible and the organization become of national scope. The governing body of the association is an executive board elected to serve initially for six months. The present members of the executive board are David Frisch, William A. Higinbotham, Joseph Keller, David Lipkin, John Manley, Victor Weisskopf, Robert Wilson and William Woodward.

The organization welcomes correspondence and sug-

gestions from scientists in all fields. Correspondence should be addressed to William N. Woodward, Association of Los Alamos Scientists, P. O. Box 1663, Santa Fe, New Mexico.

AWARDS OF THE AMERICAN SOCIETY OF MECHANICAL ENGINEERS

THE American Society of Mechanical Engineers, holding its four-day 66th annual meeting in New York on November 27, conferred its annual honors and awards for distinguished work in engineering, education, research or literature, at a dinner and honors night held at the Hotel Astor. More than 1,500 members and guests attended. Lieutenant General Ira C. Eaker, Deputy Commander, Army Air Forces, was the speaker. Alex D. Bailey of Chicago, president of the society, presided.

The medal of the society, given for distinguished service in engineering and science, was awarded to Dr. William Frederick Durand, professor emeritus of mechanical engineering at Stanford University, in recognition of his work in forwarding the design and application of principles of jet propulsion and for his effective leadership of the division of engineering and industrial research of the National Research Council, of which he is the former chairman.

The Holly Medal, presented for "some great and unique act of genius of an engineering nature," was awarded to Dr. Sanford Alexander Moss, General Electric engineer of West Lynn, Mass., for his many contributions to the development and application of turbosuperchargers to internal combustion engines.

Joseph M. Juran, professor of and chairman of the department of administrative engineering, New York University, was recognized for his contribution to the problem of quality control in mass production, and other writings, with the Worcester Reed Warner Medal, given for noteworthy contributions to engineering literature.

William Julian King, of the fuels division, Battelle Memorial Institute, Columbus, Ohio, was presented with the Melville Prize Medal for an original work, for his paper, "The Unwritten Laws of Engineering." His research is concerned chiefly with the fundamentals of combustion liquid fuels and the development of gas turbines.

Bruce Eugene Del Mar, of Santa Monica, Calif., received the junior award for his paper: "Presentation of Centrifugal Compressor Performance in Terms of Non-dimensional Relationship."

Jack Drandell, of Milwaukee, Wis., won the Charles T. Main Award for his paper entitled "Engineering in the New South."

The undergraduate student award was presented to Ensign John Waldemar Erickson, of Chicago, for his paper on "Increasing the Efficiency of Gas Turbines."

Elected to honorary membership were:

Rear Admiral Harold Gardiner Bowen, U.S.N., Naval Research Laboratory, Washington, D. C., for his service to his country: "his valiant and successful fight to introduce steam of high pressures and high temperatures into the United States Navy. The resulting performance to-day is making naval history."

Dugald Caleb Jackson, professor emeritus, Massachusetts Institute of Technology, 5 Mercer Circle, Cambridge, Mass., for outstanding leadership in education and consulting engineering fields.

Andrey Abraham Potter, acting president and dean of engineering, Purdue University, for leadership in adjusting engineering education to the needs of the war training as chairman of the ASMWT Program of the U. S. Office of Education.

Dr. Wong Wen-hao of Chungking, China, was honored *in absentia* for his preeminence in the field of professional public service, as vice-president of the Executive Yuan and Minister of Economic Affairs and head of the National Reconstruction Commission of his country.

Sir William Arthur Stanier, F.R.S., London, was also honored *in absentia*. The actual presentation had been made to him at a joint meeting of engineers in Canada recently. The award was for influencing "in an outstanding fashion the technique of railway transport."

HALF CENTURY MEMBERS

For a half century of membership in the American Society of Mechanical Engineers, fifty-year citations were awarded to the following: J. Francis Booraem, Greenwich, Conn.; George W. Colles, Rosharon, Texas; Fred H. Colvin, Point Pleasant, N. J.; William S. Conant, Washington, D. C.; Edward Richard Gnade, Oil City, Pa.; Frederick A. Goetze, New York; John W. Gray, Wayne, Pa.; Arthur M. Greene, Jr., Princeton, N. J.; George F. Hardy, New York; Albert C. Larkin, Montreal; Peder Lobben, Norway; William E. Mathews, Birmingham, Ala.; John A. Pilcher, Roanoke, Va.; Arthur Louis Rice, Wilmette, Ill.; A. M. Robeson, Marlow, England; George B. Willcox, Saginaw, Mich., and Howard E. Williams, Calumet, Mich.

THE GEOLOGICAL SOCIETY OF AMERICA

THE fifty-eighth annual meeting of the Geological Society of America will be held under the auspices of the Geological Society of Pittsburgh, on Thursday, Friday and Saturday, December 27, 28 and 29, at the Hotel William Penn, Pittsburgh.

All those attending the meetings are requested to register promptly on arriving.

The annual dinner will be held on Friday evening, December 28, at 7 o'clock in the ballroom. A complimentary dance will be arranged if this is found to be desired.

For the accompanying ladies, trips will be arranged to the "University Skyscraper," the Carnegie Museum and other points of interest in and about the city. Luncheons and other entertainments will also be provided.

If weather permits impromptu geological trips will be made. Other excursions to the Gulf Research Laboratories, the Mellon Institute of Industrial Research, the Carnegie Museum and similar points of interest may be arranged.

Local geologists will be glad to make tentative plans for informal trips. Any one interested should communicate with Dr. Charles R. Fettke, chairman of the Excursion Committee. His address is 1118 Wightman Avenue, Pittsburgh, Pa.

Associated societies which will hold meetings in conjunction with the society are as follows:

The Paleontological Society, thirty-seventh annual meeting, Secretary, H. E. Vokes, the Johns Hopkins University, Baltimore 38, Maryland.

The Mineralogical Society of America, twenty-sixth annual meeting, Secretary, C. S. Hurlburt, Jr., Department of Mineralogy, Harvard University, Cambridge, Massachusetts.

The Society of Economic Geologists, twenty-sixth annual meeting, Secretary, C. H. Behre, Jr., Columbia University, New York 27, N. Y.

The Society of Vertebrate Paleontology, fifth annual meeting, Secretary, E. H. Colbert, the American Museum of Natural History, New York, N. Y.

PSYCHOLOGICAL MEETINGS AT SAINT LOUIS

SECTION I of the American Association for the Advancement of Science and the Midwestern Psychological Association are meeting jointly in Saint Louis from March 28–30, 1946. Aside from the addresses of the vice-president of Section I and the president of the Midwestern Association, the program will be devoted to the usual papers. Abstracts in quadruplicate not exceeding 300 words in length should be sent to Dael Wolfle, Department of Psychology, University of Chicago, Chicago 37. The dead line for receipt of abstracts in Chicago is January 20. The abstracts will be turned over to a joint program committee to be announced later.

Papers will be limited to fifteen minutes in length, and ten-minute papers will also be scheduled. Any lantern slides should be included in the time limit for the paper. If a lantern is needed, this fact should be specified in the abstract. The time desired (ten or fifteen minutes) should also be noted. Each abstract should be accompanied by an additional short abstract of fifty words to be published as part of the proceedings. It should also be accompanied by a signed statement, as follows: "If this paper is accepted and placed on the program, I agree to be present in person to deliver it unless circumstances beyond my control prevent me from attending."

HAROLD E. BURTT, *Secretary of Section I, American Association for the Advancement of Science*

A TRIBUTE TO THE EDITORIAL BOARD OF THE JOURNAL OF EXPERIMENTAL ZOOLOGY

THE one hundredth volume of the *Journal of Experimental Zoology* is coming off the press. The editorial board which serves this journal and American biology merits an expression of admiration both for their service to the journal and for their truly remarkable and effective longevity.

On this board are the names of eight internationally known biologists whose contributions to scientific literature represent a distinct epoch in the history of experimental biology in America. Since the founding of the journal and the appearance of the first volume in 1904 Dr. Ross G. Harrison, who on January 13, 1946, will be 76 years of age, has served as managing editor. I am told that with the completion of the one hundredth volume he will have edited 50,000 printed pages. The other members of this board are also so well known from their scientific contributions and their influence upon American biology that what I might attempt to say here could not possibly do them justice. The main point before us is their continued function at ages far beyond that where many men not only cease to function but cease to enjoy living.

Professor William E. Castle has just passed his 78th birthday. Professor Edwin G. Conklin is now at the beginning of his 83rd year. Professor Herbert S. Jennings will be 78 years old on April next. Professor Frank R. Lillie will be 76 years old on his next birthday. The late Professor Thomas H. Morgan reached his 79th birthday in September last. Professor George H. Parker will celebrate his 81st anniversary before the new year. The only member of this board who might be considered as a veritable youth is Professor Merkel H. Jacobs, who is at the tender age of 62.

It seems extremely doubtful whether a similar record will ever be achieved again by any group of experimental biologists. They not only deserve but receive the felicitations of the entire biological world.

SAMUEL R. DETWILER

NEWS FROM ABROAD

LETTER FROM PROFESSOR MARCEL FLORKIN

Dr. Harold F. Blum, of the Naval Medical Research Institute at Bethesda, Md., has recently received a

long account from Professor Marcel Florkin, of the University of Liège, regarding the activities of himself and close associates, particularly Professors Frederieq, Bouillene, Gratia and Bacq, during the war. All these professors and their families are safe, but their story has been one of repeated flight and return, teaching and research under great difficulties, with participation in the resistance movement as a matter of course, necessitating flight into the "maquis" in some instances.

The University of Liège has suffered tremendous damage, both from the German flying bombs and the air bombings of the Allies, particularly our own. The School of Applied Sciences, the Institute de Mécanique, the Institute of Civil Engineering and the seventeenth century abbey housing the Fatigue Laboratory were all badly hit. The School of Mineralogy with its collections was burned. The School of Business Administration with its library and collections was completely destroyed. A flying bomb wrecked the building containing the laboratories of pathology, bacteriology, pathological anatomy and medical chemistry, and another struck the Institute of Physiology and Biochemistry. Still another broke all the glass in Professor Bouillene's botanical conservatory containing a large collection of tropical plants, which were all killed by the winter weather.

The whole picture is one of a great university terribly maimed, with its faculty trying to hope and to carry on with no prospect of immediate succor.

The library situation is particularly bad, as the following quotation will indicate:

> Our university had about 800,000 books in 1940. In May, 1940, when the bridges of the Meuse were blown up, the roof of the library was destroyed and the books were taken away to different shelters, among them a bank in the rue de l'Université hired for the purpose. In 1944 when the Germans set the telephone building on fire, the bank was also burned. The firemen sent a lot of water into it which came down into the cellars where the books were, with the irremediable loss of 50,000 books. And later in December a flying bomb hit another book shelter with new losses. I could not describe the present state of the accumulations of books dispersed in several places and getting slowly lost.

The story of the University of Liège seems to have been one of considerable gallantry under conditions which must many times have seemed hopeless, followed by paralyzing destruction.

> We tried to keep the university active; it was the only way to save thousands of young men from deportation to Germany; it was not easy, but we succeeded until the last moment. Then, after liberation, came for Liège the terrible months of flying bombs: more than a thousand on the city; hard days, much devastation and loss of life. When the Germans left Liège, they put the telephone building on fire and the Mineralogical Institute and collections, which were adjoining, disappeared. A few months before liberation, the finest buildings of our university had been destroyed by American bombers aiming at a nearby railway bridge. But we are free, we live again, we rebuild—but slowly! In the last days I had a narrow escape from SS murderers; M. Fourmarier too; before, he had spent one month in jail. I tried to keep the Geological Society going on, and I succeeded without any interference from the Germans.

Letter from Professor Michel Legraye

Dr. Eliot Blackwelder, of Stanford University, has received the following letter, dated November 13, from Professor Michel Legraye, of the University of Liège, Belgium:

Letter from Dr. G. H. R. von Koenigswald

A letter from Dr. G. H. R. von Koenigswald, dated Bandoeng (Java), October 23, has been received by Dr. Franz Weidenreich, of the American Museum of Natural History, New York. Dr. von Koenigswald writes:

> I am alive, and this is a great thing after three and a half years of Japanese experience! Wife and daughter are quite all right, thin and nervous, and we are very happy that we are together again!
>
> I have been a Dutch soldier during the war, and so became a POW after our capitulation. About my experiences later on: in the camp I was so lucky to belong to the translation office (Dutch-English), and so I have always been on Java in various camps in Bandoeng and Batavia. Just a few months before the Jap capitulation we came back to a terrible and overcrowded camp in Bandoeng.
>
> With the help of neutral friends most of my books and my materials have been saved. I am glad to tell you that all our fossil human skulls and jaws are still here, only one of the Mgandong skulls (skull No. IX) has been sent to Japan and is probably lost. I am so sorry that my material has not been evacuated to America, and I thank you and your friends so much for the help you offered us, and of which I heard only after our capitulation. . . . After our mobilization, when I was not any longer in the office, my native collector was dismissed, so that there was no longer any control of the important sites. I heard that the Japs have been several times in Sangiran, but it seems that nothing of any importance has been found. I hope to go to Central Java as soon as possible, and to reestablish the old collecting system, which has yielded so good results. . . .

Letter from Dr. Frank Whitmore

Dr. Weidenreich writes also that some days ago the newspapers carried a story from Tokyo that Frank Whitmore, assistant staff geologist, Mining and Geology Division, Natural Resources Section, now in Tokyo, has found in the Imperial University of Tokyo

material belonging to the site of Sinanthropus Pekinensis. According to the report, the material was removed from Peking and taken to Tokyo by the Japanese. In one of his letters to Mrs. Whitmore, the following item is of special interest:

November 8. Such excitement! We have just recovered at Tokyo University a collection of bones and artifacts from the famous Sinanthropus Pekinensis site at Choukoutien, near Peking; also the original records of Davidson Black's research here; also, the complete original plans of the excavation and their financial records, 1927–1938. We want to return all this to its owner, Peiping Union Medical College, and today I'm going to scour around to see how best it can be done.

So far nothing authentic is known of the Sinanthropus material. A representative of the Peiping Union Medical College is in Peking and is making the necessary inquiries. He has been advised by cable to communicate with Dr. Whitmore. A second representative of the college is on the way to Peking. This new message from Tokyo and the earlier one in the newspapers, apparently from the same source, may not refer to the Sinanthropus material as suggested in Dr. Whitmore's letter, but rather to material from the "Upper Cave" of Choukoutien (Upper Paleolithic).

LETTER FROM DR. EDW. MESSIKOMMER

A letter received by Dr. Wm. Randolph Taylor, of the University of Michigan, from Dr. Edw. Messikommer in Switzerland gives some information regarding Central European phycologists, from which the most important sentences may be quoted:

Wie es um die deutschen Kollegen steht, ob sie mit dem Leben davon gekommen sind, noch in Besitze ihrer Bücher, Sammlungen u. s. w. sind, darüber sind wir noch völlig im Umklaren. Es wäre jammerschade, wenn z. B. Hustedt, Krieger, Krasske nicht mehr existeren würden und ihre angefangenen Werke nicht mehr zum Abschlusse bringen könnten. Aus Prag liegen keine erfreulichen Meldungen vor. So soll sich Pascher, nachdem er seine Familie umgebracht hat, das Leben genommen haben. Czurda soll mit seiner Familie deportiert worden sein, weiteres Schicksal unbekannt.

Dr. Taylor states that Dr. Adolph Pascher was the author of many papers, a leading authority on many groups of phytoflagellates, and editor of the widely used "Süsswasserflora Deutschlands u. s. w," in many volumes. Dr. Viktor Czurda studied the Zygnematales in particular. Professor F. E. Fritsch, of Queen Mary's College, reports having heard that Dr. K. Ondraček met the same fate as Dr. Pascher. He studied the physiology of members of the Desmidiaceae.

SCIENTIFIC NOTES AND NEWS

THE Distinguished Service Award for 1945 of the American Medical Association was presented on December 5 to Dr. George R. Minot, professor of clinical medicine at the Harvard Medical School, in recognition of his work on the liver treatment of anemia. The award was made at a dinner given in his honor at the Harvard Club.

MAJOR GENERAL NORMAN T. KIRK, Surgeon General of the Army, has been awarded the Distinguished Service Medal by General Brehon Somervell, Commanding General of the Army Service Forces, in recognition of his "outstanding leadership . . . in directing the largest medical department in the history of the United States Army." In part, the accompanying citation stated, "By careful planning, efficient administration, and dynamic example he made possible extraordinary care for sick and wounded American soldiers . . . care which has never been equalled in any war."

DR. MILTON HARRIS, director of research, Milton Harris Associates, Washington, D. C., has been awarded the Olney Medal by the American Association of Textile Chemists and Colorists. It will be presented at the annual dinner of the association on January 5 at the Hotel Pennsylvania, New York, N. Y., in recognition of outstanding achievement in the field of textile chemistry.

DR. GEORGE B. DARLING, formerly president of the W. K. Kellogg Foundation, who since 1943 has been associated with the Division of Medical Sciences of the National Research Council, first as executive officer of the committees on military medicine and later as vice-chairman of the division, has been appointed executive secretary of the National Academy of Sciences and of the National Research Council.

OFFICERS for the Eastern Pennsylvania Chapter of the Society of American Bacteriologists for 1946 are as follows: *President,* Dr. Harry E. Morton, department of bacteriology of the School of Medicine of the University of Pennsylvania; *Secretary-Treasurer,* Dr. Amedeo Bodi, Jr., Temple University School of Medicine; *Counselor,* Dr. William F. Verwey, Sharp & Dohme Laboratories, Glenolden, Pa.; and *Counselor* (alternate), Dr. James Harrison, department of biology of Temple University.

THE National Malaria Society held its twenty-eighth annual meeting in Cincinnati, Ohio, on November 13–15, conjointly with the Southern Medical As-

sociation. Twenty-four papers were presented at two sessions, one of which was a joint session with the American Society of Tropical Medicine. At the business meeting, the following officers were elected for 1946: *Honorary President,* J. A. LePrince, Memphis, Tenn.; *President,* Dr. Mark F. Boyd, Tallahassee, Fla.; *President-elect,* Mark D. Hollis, Atlanta, Ga.; *Vice-president,* J. A. Mulrennan, Jacksonville, Fla.; *Secretary-Treasurer,* Dr. Martin D. Young, Columbia, S. C.

THE following is a list of those elected as officers and council of the Royal Society at the anniversary meeting held on November 30: *President,* Sir Robert Robinson; *Treasurer,* Sir Thomas Merton; *Secretaries,* Sir Alfred Egerton, Dr. E. J. Salisbury, and *Foreign Secretary,* Professor A. V. Hill. *Other members of Council:* Dr. C. H. Andrewes, Dr. W. T. Astbury, Professor P. M. S. Blackett, Dr. E. C. Bullard, Professor I. de B. Daly, Professor R. A. Fisher, Dr. C. Forster-Cooper, Professor F. E. Fritsch, Dr. S. Goldstein, Professor E. L. Hirst, Professor W. V. D. Hodge, Dr. G. M. Holmes, Professor H. W. Melville, Professor R. A. Peters, Dr. D. R. Pye, Professor S. Zuckerman.

THE University of Illinois College of Medicine began its first three-months refresher course for veterans on November 1 and is taking applications for another course to be given next February. In charge of the program are Dr. Ford K. Hick, associate professor of medicine and assistant dean in charge of postgraduate instruction in medicine, and Dr. Charles B. Puestow, professor of surgery and assistant dean in charge of postgraduate instruction in surgery. Both men have only recently been released from the Army. At the time of release, Dr. Hick held the rank of Lieutenant Colonel and was in charge of the medical service at Mayo General Hospital, Galesburg, Ill., and Dr. Puestow was a colonel and commanding officer of the Twenty-seventh Evacuation Hospital Unit, staffed largely by members of the faculty of the College of Medicine of the University of Illinois.

THE Committee on Scientific Research of the American Medical Association has made the following grants: to Barnett Sure, Arkansas Agricultural Experiment Station, effect of sulfonamides on thiamine and riboflavin metabolism; to A. R. Tunturi, University of Oregon, effect of masking tones on the responses in the cerebral cortex to pulses of pure tones; to Israel S. Kleiner and A. H. Schein, New York Medical College, nutritive value of intact protein compared with the products of its enzymatic and acid hydrolysis; to Leo L. Hardt, Loyola University, Chicago, improvements of flexi-rigid gastroscope, and to David J. Sandweiss, Thomas L. Patterson and Harry S. Saltzstein, Wayne University, Detroit, relation of endocrine glands to gastric secretion.

DR. MARION M. BROOKE resigned in June as associate professor of preventive medicine at the College of Medicine at Memphis of the University of Tennessee, to accept a commission as senior assistant sanitarian, reserve, in the U. S. Public Health Service in charge of the department of parasitology in the newly established Diagnostic and Training Laboratory of the Office of the Malaria Control in War Areas.

DR. W. H. ALLAWAY, of Lincoln, Nebr., has joined the staff of Iowa State College as research assistant professor of soils. He also will serve as agent for the U. S. Department of Agriculture with the Bureau of Plant Industry, Soils and Agricultural Engineering.

JOHN IRVIN HAMAKER, head of the department of biology at Randolph-Macon Womans College, Lynchburg, Va., after forty-one years of service, has retired from teaching with the title emeritus. Before going to Randolph-Macon College he had taught one year at Radcliffe College, two years as graduate assistant at Harvard University, and six years at Trinity College, now Duke University. Paul A. Walker has been promoted from an associate professorship of biology to a full professorship, and succeeds Dr. Hamaker as head of the department. Dr. Walker, before going to Randolph-Macon, was assistant professor of zoology at the University of Connecticut, where he had taught for six years.

DR. ALFREDO BAÑOS, JR., formerly professor of physics and director of the Institute of Physics of the National University of Mexico, has been appointed associate professor of physics at the University of California, Los Angeles. Dr. Baños served during the war at the Radiation Laboratory of the Massachusetts Institute of Technology.

PROFESSOR H. I. SCHLESINGER, professor and executive secretary of the department of chemistry of the University of Chicago, has given up his administrative work in the department as of December 1, in order to devote the greater part of his time to research, writing and to his long-standing interest in the improvement of laboratory instruction in beginning courses in chemistry. Professor Schlesinger served as secretary of the department from 1923 to 1933 under the chairmanship of Professor J. Stieglitz, and as secretary of the executive committee of the department from 1933 to date. During the past few years, he has not only carried the greater part of the administration of the department, but has also been engaged in the direction of a number of important war projects. Professor Warren C. Johnson has been appointed chairman of the department of chemistry effective on December 1. He has been at the University of Chicago since 1927 and during the past five years has been engaged in war projects of the Na-

tional Defense Research Committee and of the U. S. Engineers Manhattan District. During the past two and a half years he has been director of the division of chemistry of Clinton Laboratories, Oak Ridge, Tenn.

DR. WALLACE M. YATER, formerly chairman of the Section on Experimental Medicine and Therapeutics of the American Medical Association, has resigned as professor and director of the department of medicine at Georgetown University School of Medicine, Washington, D. C.

DR. CARL R. FELLERS, head of the department of food technology at the Massachusetts State College, Amherst, has returned to the United States. He was a major in the Army Quartermaster Corps, and for three and a half years has been on duty in the Western Pacific with headquarters at Sydney, Australia. He collaborated closely with the Australian government and scientific agencies in food production and distribution problems for the Allied Military Forces in that area.

PROFESSOR FELIX ALEXANDER VENING MEINESZ, the Dutch geophysicist, is visiting the United States on a special mission on behalf of the Netherlands Prime Minister and the Ministry of Education, Arts and Sciences. He plans to investigate the progress science has made during the war, and to discuss with American scientists an international program for the continuation of scientific collaboration.

DR. HAROLD C. UREY delivered the principal address at the inauguration on December 10 of Dr. James Creese as president of the Drexel Institute of Technology.

THE thirty-second Thomas Hawkesley Lecture of the British Institution of Mechanical Engineers was given on November 16 by Sir Edward Appleton. The address was entitled "The Scientist in War-time." It emphasized the importance of the partnership between the scientist and his service colleague.

DR. GEORGE WALD, associate professor of biology at Harvard University, will deliver the third Harvey Lecture of the current series at the New York Academy of Medicine on December 20. He will speak on "The Chemical Evolution of Vision."

DR. BART J. BOK, assistant director of the Harvard College Observatory, spoke on November 19 before a meeting of the Sigma Xi Club of the Alabama Polytechnic Institute. The title of his address was "International Relations in Science."

PROFESSOR E. V. COWDRY, professor of anatomy at Washington University, St. Louis, and director of research of the Barnard Free Skin and Cancer Hospital, will hold on December 21 a special seminar on carcinogenesis at the Tumor Clinic of the Medical Branch at Galveston of the University of Texas. Professor Cowdry also will be guest speaker at the seminar of the M. D. Anderson Hospital for Cancer Research, Houston, on December 20.

A MEETING devoted to the discussion of atomic energy and foreign policy was held in New York on December 4 by the Independent Citizens Committee of the Arts, Sciences and Professions. Among the speakers were Secretary of Commerce Henry A. Wallace, Dr. Julian Huxley, Dr. Harold C. Urey and Dr. Harlow Shapley.

THE Winter Technical Meeting of the Institute of Radio Engineers will be held at the Hotel Astor, New York, from January 23 to 26. The Radio Engineering Show will open at 4:00 P.M. on January 23. One hundred and twenty-four exhibitors have already taken the hundred and fifty booths originally planned. Efforts are being made to obtain additional space to accommodate a large list of further exhibitors. The annual banquet will be given on Thursday evening, January 24. Dr. Frank B. Jewett, president of the National Academy of Sciences, will be the principal speaker, and Edgar Kobeck, president of the Mutual Broadcasting System, will be the toastmaster. The president's luncheon will be held on Friday, January 25, in honor of Dr. F. B. Llewellyn, the incoming president. L. M. Clement, vice-president in charge of research and engineering of the Crosley Corporation, will be master of ceremonies. The institute will be host at a joint meeting with the American Institute of Electrical Engineers.

MEETINGS of the American Association of Pathologists and Bacteriologists will be held at the University of Chicago on March 8 and 9.

THIRTY-ONE technical sessions have been arranged for February 4 and 5, at the meeting in Cleveland, Ohio, of the American Society of Metals, which will have its headquarters at the Hotel Statler. A series of four educational lectures will be presented on February 7 and 8. The American Industrial Radium and the Radiograph Society will have technical sessions on February 6, 7 and 8 at the Hollenden Hotel. Headquarters for the American Welding Society will be at the Hotel Cleveland. The twenty-seventh National Metal Exposition will be held during the week in the Public Auditorium.

DR. FIRMAN E. BEAR, professor of agricultural chemistry at Rutgers University and chairman of the Department of Soils of the New Jersey Agricultural Experiment Station at New Brunswick, will address the Plant Institute of the Ohio State University on December 10. His topic will be "Intensive Agriculture in New Jersey, and Some Soil-plant Problems Related Thereto." The Plant Institute will hold

a dinner in honor of Dr. Bear at 6 o'clock on the same evening. An hour of conversation following the dinner will be led by Dr. Bear. The topic will be "Soils, Plants, Animals, Man." Dr. Bear was formerly chairman of the department of soils at the Ohio State University.

SPECIAL ARTICLES

MARIHUANA ACTIVITY OF CANNABINOL[1]

IT is generally agreed that cannabinol, the aromatic analog of the hydro-aromatic active principles of hemp oil, is entirely inactive[2] and certainly not responsible for the characteristic pharmacological activity of hemp.[3,4,5,2,6] However, conclusions are valid only within the limits of the underlying test. Bioassay of hemp components and related compounds has been limited by their scarcity and by the toxicity of the solvents necessary to obtain solution. In our earlier experiments[7] done for the purpose of comparing synthetic compounds with the highly potent natural drug principles, there was little interest in a substance when its assay indicated a potency of less than 1/200 that of charas tetrahydrocannabinol. The availability of larger quantities of cannabinol and the finding that propylene glycol is an effective solvent for intravenous preparations have made possible a study of the effects of larger doses.

Two preparations of cannabinol were employed, one (I) a repeatedly recrystallized batch prepared from the outer crust of aged charas[8] (M.P. 75.0–75.5° C),[9] the other (II) a crude synthetic cannabinol.[10,11] The amount available was sufficient for six experiments in dogs. The substances were administered intravenously in concentrated solution in propylene glycol. The results are shown in Table 1. All doses over 12.2 mg/kg produced marked ataxia. The effects are graded from I to IV in accordance with the intensity of effect as described in detail elsewhere.[7] The action was in all respects identical with that of the natural tetrahydrocannabinols. The duration of ataxia varied from two to more than 24 hours according to the dose. The results indicate a potency of about 0.04.[12] The potency of the pure substance (I) may be somewhat higher.

TABLE 1

ATAXIA ACTIVITY OF CANNABINOL IN THE DOG BY INTRAVENOUS ADMINISTRATION IN PROPYLENE GLYCOL

Sample of cannabinol	Weight of animal kg	Cannabinol		Grade of ataxia
		Dose mg/kg	Concentration gm/100 cc	
I	8.98	12.2	62	I–II
I	7.95	18.1	20	III–
II	6.56	32.5	20	IV–
II	7.80	38.5	20	III–IV
I	6.84	52.0	62	III–
I	6.60	254.0	62	III–IV

In view of the high purity of the one and the synthetic procedure by which the other was prepared, the ataxia activity of these specimens must evidently be ascribed to the cannabinol molecule rather than to an impurity. Therefore cannabinol must be included among the compounds having marihuana activity. This signifies that the end-product of the process of oxidative degradation of tetrahydrocannabinol[9] from which the cannabinol of hemp resin results, is not entirely devoid of marihuana activity. The comparatively low potency of cannabinol is of little practical significance, and even the large amounts contained in some hemp oils contribute little to the total activity because of the presence of highly potent tetrahydrocannabinols. However, the activity of cannabinol is of interest from the aspect of the relationship between structure and activity, providing one more example of the fact that under natural conditions there is not necessarily a fundamental difference between aromatic and hydro-aromatic compounds. This agrees with our prior experience that the variations in spatial arrangement due to the presence and position of a double bond in ring A, while having considerable quantitative influence upon the potency, do not determine the presence or absence of marihuana activity.[7] The activity is neither absent when, as shown previously, an aliphatic cyclohexane[13] or -heptane[7] or even a pair of open alkyl chains,[14] nor, as this study shows, when an aromatic ring takes the place of the hydroaromatic ring of the natural or synthetic marihuana-active dibenzopyran derivatives.

[1] Aided by a grant from Abbott Laboratories, Chicago.

[2] A. D. Macdonald, *Nature*, 147: 167, 1941.

[3] F. Bergel and A. R. Todd, *Biochem. Jour.*, 33: 123, 1939.

[4] A. H. Blatt, *Jour. Washington Acad. of Sci.*, 28: 465, 1938.

[5] R. S. Cahn, *Jour. Chem. Soc.*, 1933: 1400.

[6] H. Marx and G. Eckhardt, *Arch. Exp. Pharm.*, 170: 395, 1933.

[7] S. Loewe, in: "The Marihuana Problem." Lancaster, The Jaques Cattell Press. 1944.

[8] From the Narcotics Laboratory, Washington, D. C., through the courtesy of Dr. J. Levine.

[9] J. Levine, *Jour. Am. Chem. Soc.*, 66: 1868, 1944.

[10] R. Adams, B. R. Baker and R. B. Wearn, *Jour. Am. Chem. Soc.*, 62: 2204, 1940.

[11] Through the courtesy of Dr. Roger Adams, Department of Chemistry, University of Illinois.

[12] Synthetic racemic (7,8,9,10-)tetrahydrocannabinol having 1/15 the potency of charas tetrahydrocannabinol was used as a standard, as in previous studies. (See reference 7.)

[13] R. Adams, S. Loewe, B. C. Pease, C. K. Cain, R. B. Wearn, R. R. Baker and H. Wolff, *Jour. Am. Chem. Soc.*, 62: 2566, 1940.

[14] R. Adams, C. K. Cain and S. Loewe, *Jour. Am. Chem. Soc.*, 63: 1977, 1941.

Summary: Cannabinol, generally believed to be an inert component of hemp oil, is shown to have marihuana activity. The significance of this observation with regard to the relationship between structure and activity in the class of cannabinols is discussed.

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SOME EFFECTS OF SALTS ON TRUE CHOLINESTERASE

THE observations to be reported here are concerned with the effects which salts in various concentrations exert on the action of true cholinesterase at different levels of acetylcholine. Experiments have been published previously on the effects of salts on cholinesterase; their results, however, could not be fully evaluated at that time because the differentiation had not been made between the specific or true cholinesterase which hydrolyzes certain choline esters, and choline esters only, and the non-specific or pseudo-cholinesterase which is capable of hydrolyzing not only some esters of choline but a variety of non-choline esters as well.[1] The earlier discovery by Alles and Hawes[2] of differences between the cholinesterases in human erythrocytes and human serum, interesting as such and fully recognized by us,[1] did not—as recently suggested by Glick[3]—touch upon the criterion, specificity towards choline esters or non-specificity, without which no differentiation could have been made between the cholinesterases throughout the animal kingdom[4] and no basis provided for the experiments to be presented here.

Glick[5] found that the cholinesterase activity of rabbit serum, but not that of horse serum, towards acetylcholine in a concentration of 375 mg per cent. was increased by sodium and potassium chloride. We now know that rabbit serum contains predominantly true cholinesterase, and it will become clear in the course of this paper that the increase in enzymatic activity in the presence of salts was due to the increased activity of true cholinesterase.

Alles and Hawes[2] found that the cholinesterase activity of human erythrocytes, now known to contain true cholinesterase only,[1] was greatly potentiated when the sodium chloride concentration was increased. Furthermore, the curves they present demonstrate a shift in the optimum substrate concentration from 0.00025 M (4 mg per cent.) acetylcholine in the presence of 0.034 per cent. NaCl to 0.00075 M (12 mg per cent.) acetylcholine in the presence of 0.85 per cent. NaCl, though the authors make no mention of this displacement in the analysis of their results.

Recently, Nachmansohn and Rothenberg[6] reported that the cholinesterases from erythrocytes and mammalian brain, previously shown to contain true cholinesterase only,[7] display their maximum activity at acetylcholine concentrations of 0.0057 M (90 mg per cent.) and 0.01 M (160 mg per cent.) respectively—concentrations which are very much higher than those reported by Alles and Hawes and by ourselves in a former publication.[1] However, Nachmansohn employs a very high salt concentration in his medium (0.215 M.), and though at first sight his findings seem to contradict our results, actually they support them, as will be shown later in this communication.

In our experiments we determined the activity-substrate concentration curves of true cholinesterase from different sources in a medium containing 0.025 M sodium bicarbonate and also in media in which, in addition to 0.025 M sodium bicarbonate, salts in varying concentrations were present.

The enzyme activity was measured manometrically at 37.5° C. by Warburg's method, the enzyme solution being placed in the main compartment of the Warburg flask and acetylcholine in the sidearm; the total volume of the fluid, which was saturated with 5 per cent. CO_2, was 6.0 ml. A control vessel was prepared for each concentration of acetylcholine, in order to correct for spontaneous hydrolysis. The acetylcholine in the control and experimental vessels was tipped into the main compartments of the respective vessels simultaneously and readings were taken immediately after re-establishment of temperature equilibrium. In all cases the activity was calculated for a twelve-minute reaction period. Since at concentrations of acetylcholine lower than 0.001 M (16 mg per cent.) the reaction time is limited by the small amount of substrate available, it was necessary in such instances to take readings at one-minute intervals. The enzyme activity at the 0.000125 M (2 mg per cent.) acetylcholine level was obtained from the rate of hydrolysis observed after calculations had shown that one half of the original acetylcholine present in a 0.00025 M (4 mg per cent.) solution had been hydrolyzed. The figures recorded at the 0.000125 M level can therefore be considered as an approximation only.

In the sera and parotid glands of ox and sheep, in mammalian erythrocytes and in the brain tissue of any vertebrate, the specific or true cholinesterase alone is responsible for the hydrolysis of acetylcholine. The enzyme from the above sources, when measured in a medium containing no salts other than 0.025 M sodium bicarbonate, is subject to excess substrate inhibition and displays its maximum activity at low acetylcholine

[1] B. Mendel and H. Rudney, *Biochem. Jour.*, 37: 59, 1943.
[2] G. A. Alles and R. C. Hawes, *Jour. Biol. Chem.*, 133: 375, 1940.
[3] D. Glick, SCIENCE, 102: 100, 1945.
[4] B. Mendel and H. Rudney, SCIENCE, 100: 499, 1944.
[5] D. Glick, *Nature*, 148: 662, 1941.
[6] D. Nachmansohn and M. A. Rothenberg, *Jour. Biol. Chem.*, 158: 653, 1945.
[7] B. Mendel and H. Rudney, SCIENCE, 98: 210, 1943.

concentrations ranging from about 0.00015 M to 0.0005 M (2.5–8.0 mg per cent.).[1]

Fig. 1 shows the activity-substrate concentration curves obtained with mouse brain. In the absence of any salts other than 0.025 M sodium bicarbonate

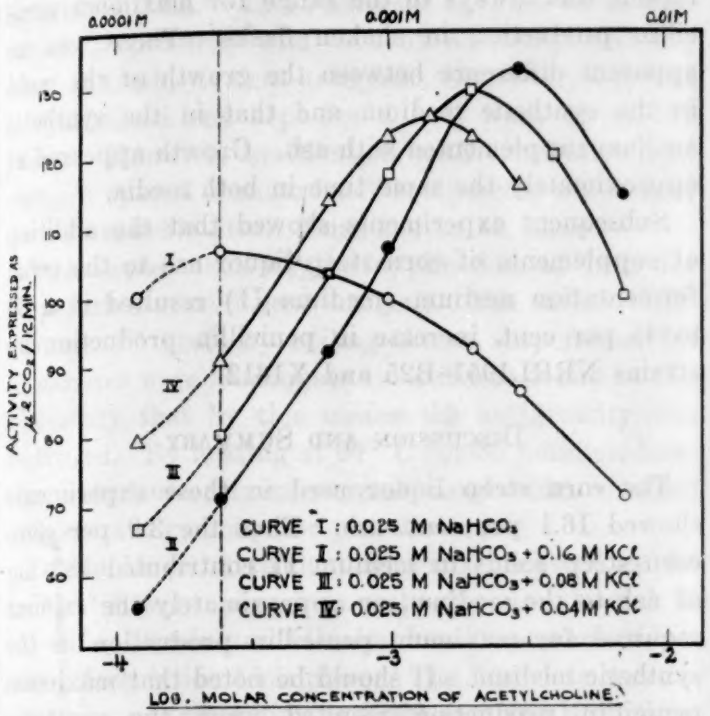

FIG. 1. Hydrolysis of acetylcholine by true cholinesterase as a function of acetylcholine concentration. The broken vertical line marks the 0.00025M (4 mg per cent.) acetylcholine level. The cholinesterase was obtained from mouse brain; 1 g of the tissue was ground and suspended in 5 ml water and 0.2 ml of this suspension was used in all experiments.

(Curve I) the optimum activity is displayed at 0.00025 M (4 mg per cent.) acetylcholine. When potassium chloride in a concentration of 0.16 M is added to the above medium (Curve II) we not only find a shifting of the region of maximum activity from 0.00025 M (4 mg per cent.) to about 0.003 M (49 mg per cent.), but also a pronounced reduction of the enzyme activity at its former optimum of 0.00025 M acetylcholine. Similar effects are obtained with lower concentrations of potassium chloride. In the presence of 0.08 M potassium chloride (Curve III) the optimum substrate concentration is 0.002 M (32 mg per cent.) acetylcholine and the activity at 0.00025 M acetylcholine, though reduced in comparison with the activity found in the presence of 0.025 M sodium bicarbonate alone, is greater than that obtained in the presence of 0.16 M potassium chloride; in the presence of 0.04 M potassium chloride (Curve IV) the enzyme displays its optimum activity at 0.0015 M (24 mg per cent.) acetylcholine, and the decrease in activity at 0.00025 M acetylcholine is still less marked than it is in the presence of the higher salt concentration.

Our experiments show that the relationship between enzyme activity and substrate concentration is changed by the addition of salt to the medium. A stepwise increase in the salt concentration, though not abolishing the excess substrate inhibition as such, causes a gradual shifting of the optimal activity of the enzyme to higher levels of acetylcholine—a fact which brings to light the cause of the discrepancy between Nachmansohn and Rothenberg's results and our own. Furthermore, with increasing concentrations of potassium chloride an absolute increase in the rate of acetylcholine hydrolysis occurs at the new optimum levels and beyond these points as well. Similar results are obtained with true cholinesterase from other sources mentioned previously in this paper.

When sodium chloride instead of potassium chloride is added to the medium in equimolar concentrations, the activity-substrate concentration curves show the same general trend but they are not identical. This fact reveals the possibility of superimposed specific effects of particular ions which will have to be studied later in detail.

The above observations point to the important role ions play in the hydrolysis of acetylcholine by true cholinesterase. The escape of potassium from cells, occurring upon stimulation,[8] might possibly help to maintain optimal conditions for the cholinesterase activity which otherwise, *i.e.*, if the potassium level in the cell remained constant, would drop sharply with declining concentrations of acetylcholine. Conversely, an increase of potassium in the extracellular fluid, shown by various workers[9,10,11] to sensitize cells to submaximal doses of acetylcholine, could cause this effect by retarding the escape of potassium from these cells, thereby creating conditions in which the activity of true cholinesterase towards low concentrations of acetylcholine would be suboptimal.

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THE EFFECT OF CORN STEEP LIQUOR ASH ON PENICILLIN PRODUCTION[1]

IT generally is assumed that corn steep liquor enhances penicillin production because of a specific organic constituent, but during a study of the physiology of *Penicillium chrysogenum* it was found that the inorganic constituents of corn steep liquor played an important role, as will be shown in the following results from preliminary studies.

[8] M. Vogt, *Jour. Physiol.*, 86: 258, 1936.
[9] W. Feldberg and A. Vartiainen, *Jour. Physiol.*, 83: 103, 1935.
[10] G. L. Brown and W. Feldberg, *Jour. Physiol.*, 86: 290, 1936.
[11] D. W. Bronk, *Jour. Neurophysiol.*, 2: 380, 1939.
[1] Published with the approval of the Director of the Wisconsin Agricultural Experiment Station.

METHODS

The penicillin fermentations were conducted in the manner described by Koffler, Emerson, Perlman and Burris[2]; the penicillin essays were made according to the method of Schmidt and Moyer.[3] The following media were used:

Medium I (synthetic medium)

	g
Lactose	20.0
Dextrin	5.0
Glacial acetic acid	4.0
NH_4NO_3	6.0
KH_2PO_4	1.5
$MgSO_4 \cdot 7H_2O$	0.25
$ZnSO_4$	0.04

Distilled water to one liter
pH adjusted to 6.0 with KOH

Medium II (corn steep liquor medium)

	g
Corn steep liquor solids	30.0
Crude lactose	30.0
$NaNO_3$	3.0
KH_2PO_4	0.50
$MgSO_4 \cdot 7H_2O$	0.25

Distilled water to one liter
pH 4.2 to 4.5, unadjusted

The inoculum consisted of 1 ml of a suspension of mold spores. The corn steep liquor solids were ashed in an electric furnace at 1400° F for 4 to 5 hours. No attempt was made to dissolve the ash before it was added to the medium.

RESULTS

Table 1 shows that supplements of corn steep ash significantly increased penicillin production by *P. chrysogenum* strains NRRL1951–B25 and X1612 in the synthetic medium. Both strains of the mold produced more penicillin in the synthetic medium supplemented with 500 mg of ash than in the usual medium containing corn steep liquor. The pH of the fermentations was always in the range for maximum penicillin production in shaken flasks. There was no apparent difference between the growth of the mold in the synthetic medium and that in the synthetic medium supplemented with ash. Growth appeared at approximately the same time in both media.

TABLE 1

THE EFFECT OF CORN STEEP LIQUOR ASH ON PENICILLIN PRODUCTION IN SYNTHETIC MEDIUM

Mold	Medium	Ash in medium	Reaction of medium, days				Penicillin, days			
			5	6	7	8	5	6	7	8
		mg/100 ml	pH				Oxford units/ml			
NRRL–	I	...	7.80	7.87	7.74	7.55	12	19	31	39
1951–		10	7.81	7.96	7.80	7.64	15	27	37	42
B25		100	7.58	7.67	7.60	7.74	34	45	50	53
		300	7.73	7.71	7.68	7.75	42	65	66	60
		500	7.71	7.70	7.70	7.84	46	73	78	77
	II	...	7.73	7.70	7.91	7.86	40	54	68	67
X1612	I	...	7.42	7.61	7.51	7.56	41	44	38	31
		10	7.40	7.60	7.46	7.49	32	34	50	52
		100	7.34	7.69	7.53	7.50	50	57	52	50
		200	7.37	7.72	8.00	7.76	78	86	91	88
		500	7.50	7.79	7.92	7.84	112	132	119	126
		700	7.56	7.77	7.78	7.70	100	105	115	100
	II	. .	7.28	7.45	7.61	7.63	69	102	96	80

Subsequent experiments showed that the addition of supplements of corn steep liquor ash to the usual fermentation medium (medium II) resulted in a 30 to 45 per cent. increase in penicillin production by strains NRRL1951–B25 and X1612.

DISCUSSION AND SUMMARY

The corn steep liquor used in these experiments showed 16.1 per cent. ash. Thus the 3.0 per cent. corn steep solids in medium II contributed 483 mg of ash to the medium, or approximately the amount required for maximum penicillin production in the synthetic medium. It should be noted that maximum penicillin production resulted when the synthetic medium was supplemented with a level of ash much greater than usually is considered necessary for normal mold growth.

The results cited above indicate that minerals play an important role in the production of penicillin. It is probable that corn steep liquor not only provides a source of nitrogen and carbon for the mold but also supplies the mineral element or combination of mineral elements necessary for optimum penicillin production. A difference in the content or balance of mineral elements may explain why some corn steep liquors are superior to others in penicillin fermentations.

A more extensive report of this work will be published elsewhere; further investigations on the role of mineral elements in penicillin production are being continued.

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[2] H. Koffler, R. L. Emerson, D. Perlman and R. H. Burris, *Jour. Bact.*, 50: manuscript in press.

[3] W. H. Schmidt and A. J. Moyer, *Jour. Bact.*, 47: 199, 1944.

HEATED, AVIRULENT ANTIGENS FOR COMPLEMENT-FIXATION TESTS WITH CERTAIN ENCEPHALITIS VIRUSES[1]

THE increasing application of the complement-

[1] This study was carried out under the Commission on Neurotropic Virus Diseases, Board for the Investigation

fixation test for the diagnosis of several human encephalitides compels attention to the use of avirulent antigens, since certain active ones may possibly induce disease through accident or carelessness. Avirulent antigens can be prepared by means of ultraviolet light irradiation.[2] These antigens have the same antigenicity, specificity and lack of anticomplementary effect as fresh, virulent antigens. Moreover, they can be lyophilized and kept for a long time, up to two years.[3] However, inactivation with ultraviolet light requires special standardized equipment, which may not be available at all times and in all places.

Tests were made on the application of heat for preparation of avirulent antigens. The earlier "koktoantigens"[4] made by boiling brains suspensions for 30 minutes were inadequate since it was found in this laboratory that by this means the antigenicity was destroyed. By heating at 60° C for 30 minutes, however, avirulent antigens were obtained which retained sufficient antigenicity for practical use.

Ten to 15 cc of virulent antigens prepared as described,[3, 5] were placed in test-tubes and heated at 60° C for 30 minutes. During heating a more or less heavy flocculation took place. The flocculate was removed by centrifugation at 2,500 rpm for 10 minutes in a horizontal centrifuge, or at 6,000 rpm for 30 minutes in an angle head centrifuge. The supernate constituted the antigen, which could be lyophilized.

Heated antigens derived from the following viruses have been tested: St. Louis, Japanese B and Russian spring-summer (Far Eastern) encephalitis viruses; louping-ill and West Nile viruses; Western, Eastern and Venezuelan equine encephalomyelitis virus. The results of the tests are shown in Table 1.

The specificity of the heated antigens tested by cross-reaction was found to be unchanged and the same as that of unheated, virulent antigens. Furthermore, they had not acquired thereby any anticomplementary effect. The tabulated results show that although a loss of antigenic titer was correlated with heating, the antigenic titer after heating was sufficiently high for the viruses of Japanese B, Russian spring-summer and West Nile encephalitis for safe use. The heated antigens of louping-ill and Western equine encephalomyelitis viruses were somewhat lower but still usable; St. Louis and Eastern equine encephalomyelitis viruses could be employed sometimes, *i.e.*, if the initial titer could be made sufficiently high. The Venezuelan equine virus antigen after heating was ineffective. By test, lyophilization of heated antigens did not reduce their titer; they could therefore be handled for preservation or transportation in the same way as the irradiated antigens.

TABLE 1

ANTIGENS HEATED AT 60° C FOR ½ HOUR AND CENTRIFUGED

Antigen of virus of	LD_{50} titer before heating	Mouse inoc. with undiluted heated antigen	Complement-fixing titer of antigen	
			Before heat	After heat
St. Louis encephalitis	10^{-4}	0/10*	1:4	1:2
			1:16	1:2
Japanese B (Nakayama strain) encephalitis	$10^{-1.5}$	0/5	1:64	1:32
			1:128	1:16
	$10^{-3.5}$	0/10	1:16	1:8
			1:64	1:8
Russian spring-summer encephalitis	10^{-7}	0/5	1:16	1:8
	10^{-5}	0/10	1:32	1:16
Louping-ill	10^{-3}	0/10	1:16	1:4
West Nile disease	$10^{-4.5}$	0/10	1:64	1:32
Western equine encephalomyelitis	10^{-5}	0/5	1:64	1:8
	$10^{-6.5}$	0/10	1:32	1:4
Eastern equine encephalomyelitis	$10^{-6.5}$	0/10	1:2	0
			1:16	1:4
Venezuelan equine encephalomyelitis	$10^{-7.5}$	0/10	1:2	0
			1:8	0

* Fractions represent number of mice dead of virus infection over number used.

Summary. A simple method is described for producing avirulent mouse brain antigens for complement-fixation tests in human encephalitides, by application of heat at 60° C for 30 minutes. The heated antigens retain for most of the viruses employed a sufficiently high titer to warrant their use, since they are also specific, not anticomplementary, can be lyophilized and moreover, are avirulent, and thus can be handled with safety.

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and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Service, Office of the Surgeon General, U. S. Army.

[2] J. Casals, *Proc. Soc. Exp. Biol. and Med.*, 49: 501, 1942.

[3] J. Casals, SCIENCE, 97: 337, 1943; *Jour. Bact.*, 50: 1, 1945.

[4] S. Nakagawa, *Z. Immun.-Forsch.*, 39: 563, 1924; J. Takaki, A. Bonis and O. Koref, *Z. Immun.-Forsch.*, 47: 431, 1926.

[5] J. Casals and R. Palacios, *Jour. Exp. Med.*, 74: 409, 1941.

THE RATE OF WATER LOSS FROM THE RESPIRATORY TRACT OF MAN LIVING IN A SUBTROPICAL CLIMATE[1, 2]

NEAR the turn of the century direct measurements of water loss from the lungs were made by Galeotti and his associates,[3] Weyrich,[4] Loewy and Gerhartz,[5]

[1] From the Department of Medicine, Tulane University, School of Medicine and Charity Hospital, New Orleans.

[2] Aided by a grant by the Rockefeller Foundation and Helis Institute for Medical Research.

[3] G. Galeotti and E. Signorelli, *Biochem. Zeitschr.*, 41: 269, 1912; *Arch. f. d. ges. Physiol.*, 160: 27, 1914–15; *Biochem. Zeitschr.*, 46: 173, 1912.

Benedict and Benedict[6] and more recently, in a limited number of subjects, by Seeley.[7] Most of these methods are cumbersome and difficult to use, and in no instance was the accuracy of the method adequately determined. Furthermore, the discrepancies in results rendered the data difficult to interpret.

A new and simple gravimetric method, condensing the expired water in cold aluminum coils for weighing, has been developed for the measurement of the rate of water loss from the respiratory tract of man.[8] The method has a mean accuracy of 0.3 per cent., range ±1.27 per cent., or a mean error of about 27 mg when collecting 1,000 mg (approximately the amount collected from each subject) of water.

In a study of 107 normal young adults of both sexes and White and Negro races (ages 17–43, all except four below 30 years) resting in a comfortable environment (room temperature 20.0–21.1° C.; relative humidity 55–60 per cent.) the rate of water loss from the respiratory tract was:

Mean, 0.878 ± 0.030 gram/m²/10 min.[9]
Range, 0.527 to 1.172 grams/m²/10 min.
Standard deviation, 0.333 ± 0.021 gram/m²/10 min.
Coefficient of variations, 37.90 ± 2.49 per cent.

There was no significant difference in sex or race.

The rate of water loss correlated highly with the rate of irrigation of the respiratory tract with air, the correlation coefficient being $+0.91 \pm 0.02$. A repetition of the studies in a hot month of August, 1944, in New Orleans and cool month of January, 1945, showed no significant seasonal differences. The rate and depth of respiration influenced the rate of water loss more or less in proportion to the rate of irrigation of the respiratory tract with air, although after correcting for the rate of irrigation of the lungs with air, the rate of water loss was greater when the respirations were slow and deep. Slow and deep respiration allows more time for evaporation of water into the inspired air. Exercise increased the rate of water loss, an influence due in a large part to the increased rate of ventilation of the lungs.

Cool foggy (temperature 15° C.; relative humidity 97 per cent.) or cool, dry (temperature 15° C.; relative humidity 60 per cent.) room air (inspired air) influence the rate of water loss relatively little while hot dry (50° C. and 18 per cent. relative humidity) increased the rate of water loss and a hot moist (50° and 49 per cent. relative humidity) reduced the rate of water loss considerably. The marked reduction in the water loss when inspiring hot moist air is due in a large part to the influence of cooling of air inspired (from 50° C. to about 39° C.) by the respiratory tract. This cooling at high temperatures increases markedly the relative humidity of the inspired air, thus reducing its capacity to hold more water. The relative magnitudes of absolute humidity of the air before and after inspiration and expiration are of more importance in understanding water loss than the relative humidity of either inspired or expired air considered separately.

When in a comfortable environment (*vide supra*) the mean temperature of the expired air was 33.19 ± 0.21° C., extremes 31.6 and 34.2 and the mean relative humidity 88.15 ± 1.31 per cent., extremes 78 and 96. The expired air, therefore, is not saturated. Its temperature and relative humidity varied with the conditions of air inspired. Inspiration of cool dry or cool foggy (*vide supra*) air influenced these very little. Inspiration of hot dry and hot moist room air (*vide supra*) influenced the temperature and relative humidity of the expired air considerably. The temperature of the expired air was greater than body temperature but cooler than the inspired air. The relative humidity of the expired air was lower than that when cool air was inspired. The degree of change was influenced by the warmth and wetness of the air inspired. For example, inspiring air at 50° C. and a relative humidity of 18 per cent. resulted in expired air at about 39° C. and about 76 per cent. relative humidity. When inspiring air at 50° C. and 49 per cent. relative humidity the expired air had a temperature of about 39.4° C. and relative humidity of about 74 per cent.

Therefore, the rate of water loss from the respiratory tract and the temperature and relative humidity of the expired air depend upon the conditions of the air inspired and the nature of respiration. Expired air is not and can not be saturated with water.

These studies of water loss and heat loss from the respiratory tract will be published in detail elsewhere.[8,9]

An appreciation is extended to Mr. G. Morgavi for his valuable technical assistance.

G. E. BURCH

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[4] W. Weyrich, Beohachtungen ober die unmerkllche Wasseransschiedung der Lungen und ibr Verhältniss zur Hautperspiration. E. J. Karon, Universitäts-Buchbandier, Dorpat, 1865.

[5] A. Loewy and H. Gerhartz, *Pflug. Arch. Physiol.*, 155: 231, 1914.

[6] F. G. Benedict and C. G. Benedict, *Biochem. Zeitschr.*, 186: 278, 1927.

[7] L. E. Seeley, *Trans. Am. Soc. Heat. Vent. Eng.*, 46: 259, 1940.

[8] G. E. Burch, "A Study of Water and Heat Loss from the Respiratory Tract of Man. Methods: I. A Gravimetric Method for the Measurement of Water Loss. II. A Quantitative Method for the Study of Heat Loss." To be published.

[9] The rates of water loss are all in grams per square meter of surface area of the body per 10 minutes.

[10] *Idem*, "Water and Heat Loss from the Respiratory Tract in Normal Subjects in a Subtropical Climate." To be published.

FLOWER FORMATION IN THE PINEAPPLE PLANT AS CONTROLLED BY 2,4-D AND NAPHTHALENEACETIC ACID

THE flower-inducing power of appropriate growth-regulating substances in the pineapple plant may be ranked among the most spectacular effects of plant hormones. The treatments as given here in Puerto Rico resulted in flower formation with a precision and uniformity of response (Fig. 1) comparable to

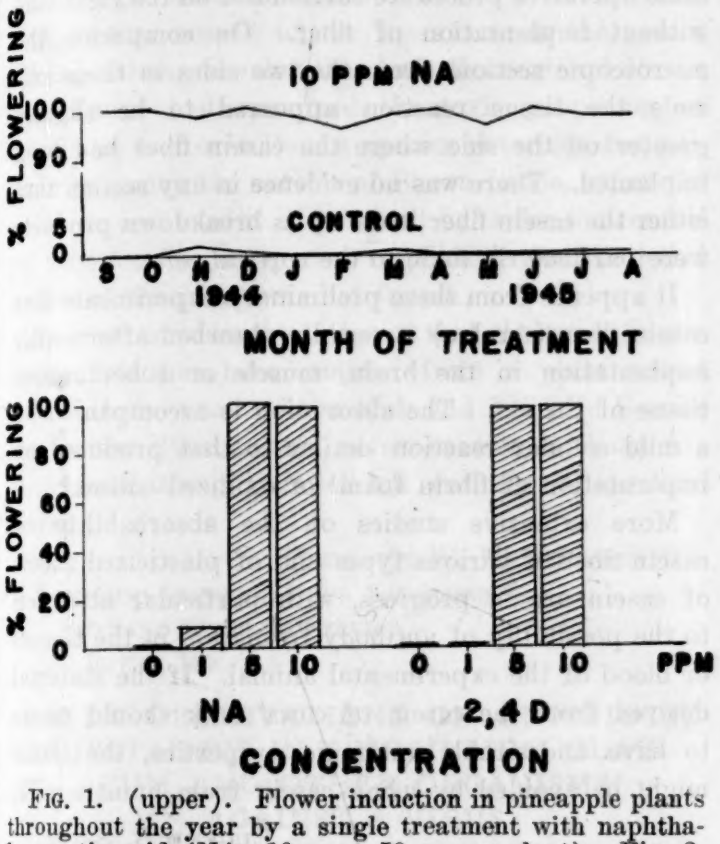

FIG. 1. (upper). Flower induction in pineapple plants throughout the year by a single treatment with naphthaleneacetic acid (NA; 10 ppm, 50 cc per plant). Fig. 2. (lower). Flower induction as a function of the concentration of NA and 2,4–D, applied by a single treatment in July, 1945, when the plants were 22 months old. Flowers were visible 6 to 8 weeks after treatment. The plants, of the Cabezona variety, were 16 months old in January, 1945. Each valve represents observations on from 40 to 50 plants.

that of the classical avena test for auxins. Flowers, which later produced perfect fruits,[1] were induced in plants which were not due to flower for another year or more. These results were somewhat surprising, since it had been shown previously in Hawaii[2] with the Cayenne variety and in Florida[3] with the Abachi variety, that naphthaleneacetic acid will induce flowering from 6 weeks[3] to 4 months[2] ahead of the natural flowering time. In addition it was shown that the plants in Florida did not respond during the summer. The investigations reported here, however, show that with the Cabezona variety growing in the dry Lajas Valley of Puerto Rico, growth-regulating substances will cause flower formation throughout the year (Fig. 1).

Although the main experiments were performed with naphthaleneacetic acid (NA), 2,4-dichlorophenoxyacetic acid (2,4-D) was also tested throughout the year. The results show that both substances are equally effective for the flower induction in pineapples. A concentration of 5 parts per million (50 cc per plant, applied in the center, equivalent to 0.25 mg per plant) is sufficient to cause a 100 per cent. response (Fig. 2).

The following conclusions may be drawn from these observations.[4]

(1) One ounce of either NA or 2,4-D is a sufficient amount for inducing flowering in 113,000 plants, which is equivalent to a pineapple plantation of 11 acres.

(2) One dollar's worth of chemical (2,4-D, at the current price of $7.50 per kg) will treat over one-half million of plants (536,000), the equivalent of 53 acres of pineapples.

It is also of interest to note that the same 2,4-D which is now being widely applied as a selective herbicide, is an equally effective flower-inducing agent for the pineapple when used in 100 times lower concentrations.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A NEW ABSORBABLE MATERIAL FOR USE IN NEUROLOGICAL AND GENERAL SURGERY

THERE have been reports in the recent literature on the properties and uses of readily absorbable materials in surgical procedures.[1, 2, 3] The substances described are human fibrin foam and oxidized cotton. Particular emphasis has been laid on the value of such agents in brain surgery, especially in the control

[1] The size of the fruit depends on the size of the plant; no effect of hormone treatment on the flavor of the fruit could be detected; J. van Overbeek *et al.*, Ann. Rept. Inst. Trop. Agric. Puerto Rico, 1944–45, in press. Here also the advantages of the "hormone method" over the "carbide method" have been pointed out.

[2] H. E. Clark and K. R. Kerns, SCIENCE, 95: 536–537, 1942.

[3] W. C. Cooper, *Proc. Am. Soc. Hort. Sci.*, 41: 93–98, 1942.

[4] A more detailed report will be published elsewhere.

[5] The author is indebted to Mr. Guillermo Dávila Olivo and Mrs. Elba Santiago de Váquez for their assistance, and also to Dr. A. Ortiz Romeu, who generously made available part of his plantation for experimental purposes.

[1] F. D. Ingraham, O. T. Bailey and F. E. Nulsen, *Jour. Neurosurg.*, 1: 171, 1944.

[2] V. K. Frantz, *Ann. Surg.*, 118: 116, 1943.

[3] T. J. Putnam, *Ann. Surg.*, 118: 127, 1943.

of bleeding. For this purpose, the absorbable material is soaked in a solution of thrombin and applied to the bleeding surface. The thrombin usually causes prompt clotting. The advantage of using one of the new substances, rather than a cotton pledget, lies in that fact that a pledget made of absorbable material need not be removed before closing the wound. This prevents the recurrence of bleeding which follows the removal of cotton. The field of usefulness of such substances in the realm of general surgery, too, is wide.

In considering various substances for use in absorbable sponges, batting, thread, etc., one of us (M. Z.) proposed casein fiber prepared from milk. Such fiber, from cows' milk, has been used commercially for some years in textiles under the trade name of "Aralac."[4] It is plentiful, inexpensive, extremely uniform chemically, and has physical properties which recommend it for the present purpose. It is readily spun into thread, forms an easily manipulated batting, and can be steam-sterilized repeatedly and stored indefinitely.

In preliminary experiments here reported, pledgets of Aralac batting (30–150 mg total dry weight) were inserted into the subcutaneous tissue, temporal muscle, subdural and subarachnoid spaces and the substance of the brain itself in a series of six cats. Each operation was performed aseptically under sodium pentobarbital anesthesia, and the animals were allowed to survive for 11, 11, 12, 23, 35 and 46 days, respectively. At the end of these periods, the animals were anesthetized and the brains removed along with other tissues that had been in contact with the batting. None of the animals showed any ill effects from the insertion of the casein fiber, and each was in good health at the termination of the experiment.

At post-mortem, no Aralac was visible grossly in any specimen. Microscopically small amounts of the fiber remained in the three animals that were examined after 11 and 12 days. A few of the fibers seen were bordered by giant cells. The principal tissue reaction consisted of the presence of macrophages or, in a few instances, polymorphonuclear leucocytes and lymphocytes on the one hand, and fibroblastic and endothelial cell proliferation on the other. In the three cats which were allowed to survive the longest, no trace of fibers remained. Giant cells were very rarely found in the sections from these animals. The tissue reaction consisted chiefly of fibrous tissue proliferation and the presence of macrophages at or near the site of implantation.

In two of the experiments (11 and 12 days), the casein fiber was implanted on the left side and the same operative procedure carried out on the right side without implantation of fiber. On comparing the microscopic sections from the two sides in these animals the tissue reaction appeared to be slightly greater on the side where the casein fiber had been implanted. There was no evidence in any section that either the casein fiber itself or its breakdown products were particularly toxic to the cortical cells.

It appears from these preliminary experiments that casein fiber (Aralac) is rapidly absorbed after septic implantation in the brain, muscle or subcutaneous tissue of the cat. The absorption is accompanied by a mild cellular reaction similar to that produced by implantation of fibrin foam[1] or oxidized cotton.[2]

More extensive studies on the absorbability of casein fiber of various types and of plasticized sheets of casein are in progress, with particular attention to the possibility of antibody formation in the tissues or blood of the experimental animal. If the material derived from the casein of cows' milk should prove to have undesirable antigenic properties, the latter might be avoided by using casein from human milk.

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[4] The Aralac used in these experiments was kindly furnished by Aralac, Inc.

DISCUSSION

A NOTE ON THE NATURAL OCCURRENCE OF FLUOROACETIC ACID, THE ACID OF THE NEW RODENTICIDE "1080"

IN a recent article[1] the discovery of the value of sodium fluoroacetate, referred to as compound "1080," as a highly successful rodenticide by the joint work of the Economic Investigations Laboratory and the Wildlife Research Laboratory of the Fish and Wildlife Service is described. Subsequent to this publication, the writer and his colleagues learned of the work

[1] E. R. Kalmbach, SCIENCE, 102: 232, 1945.

of Marais[2] who investigated the toxic principle of *Dichapetalum* (*Chailletia*) *cymosum* (Hook) Engl., called "Gifblaar" and known as one of the most poisonous plants of South Africa. Following the previous attempts by Steyn[3] and Rimington,[4] Marais succeeded in the isolation of a toxic substance and identified it as fluoroacetic acid. The high toxicity of this fluorinated acid led him to suggest that the simple fluorinated organic acids might be a source of valuable poisons and insecticides.

A further search of the literature on the genus, Dichapetalum, revealed that both Renner[5] and Power and Tutin[6] had examined the toxic properties of *Chailletia toxicaria* Don, a species notorious for poisonings among the natives of Sierra Leone, where the colonists had used it in poisoned baits for the control of rats, but the compound responsible for the lethal action of the plant was not found.

It is of considerable interest that the toxic fluoroacetic acid has been isolated from a plant source and that the work of the Fish and Wildlife Service on sodium fluoroacetate as an economic poison has progressed along parallel but entirely independent lines.

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EARLY OBSERVATIONS ON ANTIBIOTIC SUBSTANCES IN PENICILLIUM GLAUCUM AND OTHER ORGANISMS AGAINST A VIRUS

THE quotation cited below was stumbled upon by the author, whose field is far removed from antibiotics, and is given for the benefit of the many hunters in the field of antibiotics.

The quotation is from a Russian paper by M. G. Tartakovskii, entitled "Ekssudatny tiff ili chuma kur" ("Exudative Typhus or Fowl Plague), published in *Arkhiv Veterinarnyki Nauk* (*Archives of Veter. Sci.*) v. 34 (1904), pp. 545–75, 617–66. The quotation following is from p. 642:

> Maggiora and Valenti report a mould contaminant that destroyed fowl plague contagion in a test-tube containing blood (mixed with a physiologic solution of NaCl) of a chicken that died of the disease. The kind of mould is not stated by the authors. I observed that under the influence of *Penicillium glaucum* the contagion of exudative typhus was destroyed if the blood was diluted in a physiologic solution of NaCl. Thick blood in a test-tube, covered with a heavy growth of mould, remained virulent.
>
> Especially instructive are the experiments of Centanni. If blood of chickens that died of fowl plague were added to bouillon media and inoculated with the intestinal bacteria of chickens (a form of *B. coli communis-Bacterium coli gallinarum*, which easily penetrates into the organs and blood and infrequently has given occasion to false discoveries) the contagion of exudative typhus perished within 24 hours. Centanni explained the rapid loss of virulence of excrements from birds that died of fowl plague due to the destructive action of the intestinal rods.
>
> It is possible that the action of intestinal bacteria hindered even intravitam accumulation of large numbers of microbes of fowl plague in the intestines, especially in the lower sections where *B. coli* is found in large numbers and where best conditions prevail for its development. Only in the intestinal form of fowl plague, when the local infection is the strongest, there is a prevailing accumulation of fowl plague microbes over the intestinal.
>
> It is interesting that, according to Centanni, a culture of bacilli of fowl cholera, under conditions described as *in vitro*, also destroyed the contagion of fowl plague.

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DANGERS INHERENT IN SCATTERED CATHODE RAYS

AN incident which occurred in the department of radiology at the Massachusetts General Hospital in December, 1944, is particularly pertinent at the present time inasmuch as it has to do with burns caused by scattered cathode rays.

Six men, after very brief exposure to scattered electrons from a 1,200 kilovolt electrostatic generator which was under repair, experienced burns of varying severity. These burns had certain similarities to, but differed from, x-ray reactions, sunburn and thermal burns. Certain factors characterized them, one being an apparently limited depth of penetration. (Relatively thin layers of clothing appeared to stop many of the electrons.) The burns showed three distinct phases of reaction, the latter phases making their appearance as the earlier ones were healing. The second and third phases developed both in areas previously uninvolved and in old healing areas.

The extent of scattering of cathode rays had not been appreciated, nor had the medical literature contained articles dealing with that phase of cathode irradiation. In order that this experience at the Massachusetts General Hosiptal may not be duplicated, publication of a detailed account seems necessary, and this report will appear in the January, 1946, issue of *Radiology*.

LAURENCE L. ROBBINS

[2] J. S. C. Marais, *Onderstepoort Jour. Vet. Sci. Animal Ind.*, 18: 203, 1943; 20: 67, 1944.
[3] D. G. Steyn, "Digest of Vet. Education and Research," 13th and 14th Reports, Part 1, 187, 1928.
[4] C. Rimington, *Onderstepoort Jour. Vet. Sci. Animal Ind.*, 5: 81, 1935.
[5] Renner, *Jour. African Soc.*, 1904: 109.
[6] F. B. Power and F. Tutin, *Jour. Am. Chem. Soc.*, 28: 1170, 1906.

SCIENTIFIC BOOKS

COAL UTILIZATION

Chemistry of Coal Utilization. By H. H. LOWRY, editor, and a staff of 35 contributors. 2 volumes—Volume 1, pages 1–920; Volume II, pages 921–1868. New York: John Wiley and Sons, Inc. 1945. The set, $20.00.

No reviewer could be fully competent to review the two-volume treatise on coal and its utilization which the present work comprises. It was prepared under the auspices of a committee of the National Research Council over a period of eight years. The committee outlined the proposed review in 1938–1939, drew up a list of competent collaborators, collected all the contributions, sent these (until 1942) to two reviewers for criticism, thence to the author for reconsideration. Since 1942, the editor himself appears to have shouldered much of the responsibility for review of the texts as they were received, the reading of galley and page proof, preparation of the extensive book, name and subject indexes, corrections of incomplete or incorrect references, and the changes necessary to secure greater uniformity of style. The contract between the National Research Council and the publishers was drawn up with no royalties either to the council or the contributors to secure the lowest possible price for the report, and the costs of preparation of manuscript and illustrations were borne by the publishers and by a generous contribution from the Koppers Company. There results from these unselfish efforts on the part of all concerned a unique, comprehensive and critical review of the vast literature of coal and its utilization, never hitherto available in any language. Scientists and technologists in every phase of modern industry are under deep obligation to all those who have contributed to this outstanding effort.

Twenty-five years ago the writer made a picayune attempt to formulate the scientific aspects of fuel production and utilization in a small volume intended to cover the ground which has here been so comprehensively covered. To read from the finished product which these two volumes represent the current state of the science and technology of coal makes one realize two things: one, the temerity of a youthful author in 1920, and, secondly, the tremendous strides that have been taken in the intervening years to place the whole subject of coal utilization on a permanent, sound, scientific basis.

The first volume deals with the origin and classification of coal, its physical properties, such as hardness, strength, plastic swelling and other properties, its constitution as determined by halogenation, oxidation, reduction, hydrolysis reactions, the sulfur, nitrogen and mineral contents, the cleaning, water content and storage changes of coal and the action of solvents and temperature on the coal substance. Here are 24 chapters occupying nearly 900 pages of double columns with hundreds of diagrams and tables of data.

The second volume deals in 16 contributions with the gases, sulfur and nitrogen compounds, light oils and tar that result from coal carbonization, together with the combustion process in fuel beds, in pulverized coal, in the manufacture of producer and water gas. Direct generation of electricity from coal and gas (fuel cells) is reviewed with mainly pessimistic conclusions. The final three contributions deal with hydrogenation of coal and tar, synthesis of hydrocarbons and of alcohols from water gas.

A reviewer has to be eclectic in a survey of such size unless he has to spend several months in a detailed reading of such a work. He naturally turns to those phases of the work in which he himself is most interested and conversant with the subject-matter treated. The 15 to 20 per cent. sample that this reviewer has thus made gives him complete confidence that readers in the other areas will be completely convinced that, through the efforts of editor, contributors, publishers and the National Research Council, the science and technology of coal have here been accorded that outstandingly authoritative and comprehensive treatment that the Committee on Coal Utilization set before themselves as a goal. We are all, I repeat, deeply in their debt.

HUGH S. TAYLOR

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METEOROLOGY

Descriptive Meteorology. By HURD C. WILLETT. Illustrated. viii + 310 pp. Academic Press, Inc. 1944. $4.00.

DESCRIPTIVE METEOROLOGY is an elementary text-book designed for an undergraduate course in meteorology, where the students have a knowledge of calculus and general physics. The author's main purpose in writing the book was to provide a text-book for his own course, and he has purposely omitted or given little attention to a number of topics which he believed unimportant in a course of this type.

The book begins with a general outline of the topics which are to be presented; this is followed with a set of definitions of various meteorological elements. With the foregoing as an introduction, it then takes up the eleven general topics which, as indicated in

the preface, include the material that the author thinks should form the basis for an elementary descriptive course in meteorology. These can best be summarized by listing the chapter headings and adding a few comments where the chapter headings need to be supplemented.

The first five topics are concerned with the basic principles of meteorology and provide the background for the descriptive material presented in the remaining portion of the book. These five topics are: (1) "The Composition and the Vertical Extent of the Atmosphere," in which the hydrostatic equation is also introduced and integrated; (2) "Adiabatic Processes and the Vertical Stability of the Atmosphere," which also includes a discussion of adiabatic diagrams; (3) "The Heat Balance of the Atmosphere and the Explanation of the Observed Temperature Distribution"; (4) Evaporation and Condensation in the Atmosphere"; (5) "Wind Velocity in the Atmosphere."

The latter half of the book is given over to the remaining six topics, which fall into a class generally referred to as synoptic meteorology. These six topics are: (1) "The General Circulation of the Earth's Atmosphere," which also includes a discussion of "high and low index" conditions; (2) "The Secondary Circulations of the Thermal Direct Type," where a detailed description of hurricanes is also given; (3) "Air Mass Characteristics"; (4) "Secondary Circulations of the Dynamic Type," which mainly discusses fronts and wave cyclones; (5) "The Tertiary Circulations"; and (6) "The Synoptic Representation of Current Weather and the Forecasting of the Future Weather," where the author gives a few examples of weather analysis and merely surveys the field of weather forecasting.

For the most part, the equations presented are derived from first principles. No derivations, however, are given for the formulas for specific humidity and mixing ratio. In the case of mean molecular weight of air, the method by which the value is determined is not given. It is believed that the addition of the foregoing would be very useful to the reader in understanding these concepts.

Some material has been omitted which most meteorologists would probably want included in a text of this nature. No mention is made, for instance, of wet-bulb temperature, equivalent-potential temperature, snow pellets and small hail. Occasionally technical terms with which the beginning student would not be familiar are introduced with insufficient discussion. These include such terms as front, frontogenesis, entropy, convergence and divergence.

The description of a hypothesis for the development of hurricanes and the material on air mass characteristics are given in great detail, probably in greater detail than is necessary in an elementary book, but little mention is made of the weather and the causes of weather in the tropics. The intertropical front, or convergence zone, and wave disturbances in the easterlies are given no attention. In describing the characteristics of occluding wave disturbances, a large amount of material is included concerning the developments at the surface, but completely lacking is a description of developments aloft except for that which concerns frontal structure. These are considered to be important omissions.

One might object to the phrase, "the capacity of air to hold water vapor," as it is misleading; to the rather unusual integration of the hydrostatic equation; or to the statement, "the particle rises along its own particular dry adiabat," instead of, the particle cools at the dry adiabatic rate. Some would probably consider these to be rather minor objections.

In spite of the above criticisms, it is believed that this text is of much value, as it is one of the few meteorological texts designed for use in undergraduate courses where the students have had preparation in college mathematics and physics. The author has purposely not attempted to cover the field of weather forecasting in a chapter or two, as has been done in numerous elementary texts, and for this he is to be complimented. The subject-matter is well integrated, giving the book good continuity.

The book as a whole gives the impression that the author has published it only after much thought and careful preparation, and it is indeed a welcome contribution from the standpoint of those concerned with meteorological education. It should prove very useful to people giving courses on the level for which the book has been prepared.

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PLANT GROWTH

Plant Growth. By L. EDWIN YOCUM. 192 pages. 16 plates. Cloth. Lancaster, Pa.: The Jaques Cattell Press. 1945. $3.00.

IN the words of the author, "This book has been written in an attempt to bring together the knowledge necessary to answer (as far as possible) the many technical questions which the plant lover may ask about growing plants. It is an attempt to make clear the 'how and why' of plant growth. The principles of the laws of nature as applied to plants growing in the soil are stressed. Many of the newer theories used in plant culture are described; others, not so well established, are suggested as possible future developments.

The illustrative material has been selected, when possible, because it is found around most homes, and can be examined by the reader."

Written for the layman, this book describes processes of plant growth from the time of seed germination through the fruiting stage. It contains morphological descriptions of the organs of the plants with a brief account of their functions. The main portion of the book deals with the physiological relations of the plant to its environment. Material on the absorption of water and minerals, photosynthesis and transpiration, is handled in a standard way with practical suggestions. The practical aspects of grafting, budding, propagation, mulching, soil improvement, weeds, entomology and plant diseases are described. The author endeavors to give the reader an intelligent approach to his own problems and an appreciation of scientific aspects of plant study.

A comprehensive account of Mendel's work on the pea introduces genetics and aids in the following discussion on heredity and variation of plants. In fact, this part is well told in succinct detail. To each chapter is attached a list of references that may interest the individual who is more curious about the various phases of the plant. These not only include the standard botanical texts which are found in high-school and college classrooms and libraries but the *Botanical Review* and the publications of the U. S. Department of Agriculture which bring the references up to date. The book is readily understandable and will be welcomed by lay readers interested in a non-technical description of recent advances in our knowledge of plant growth. This book promises to be a very successful member of the publisher's series of texts for popularization of science. The format is attractive, the text is accurate and the style is interesting, dignified and free of the all too frequent attempts to sensationalize the importance of recent research.

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BOVINE TRICHOMONIASIS

Bovine Trichomoniasis. A Monograph on *Trichomonas foetus.* By BANNER BILL MORGAN. 150 pp. Illustrated. Minneapolis, Minn.: Burgess Publishing Co. 1945. $3.25.

Trichomonas foetus infects the bovine genital tract of both sexes and lowers fecundity. Thus the disease has an immediate effect on milk production and eventually limits the supply of beef. In view of war-time experiences with rationing of these foods the timeliness of the author's monograph needs no emphasis. In addition, the disease is venereal and from the cattle raiser's standpoint this is its most serious aspect since the bull, having a value "equal to that of half of the herd" must be sacrificed with the consequent loss of invaluable hereditary qualities.

A remarkable feature of the literature on *T. foetus* is its recent appearance. Of 408 citations by the author of the monograph all but 3 were published since 1925. Failure to discover the importance of genital trichomoniasis prior to that time was due in part to a general misconception concerning *Brucella abortus* (Bang, 1897), which was regarded as the sole causative agent of bovine infectious abortion. Success in demonstrating the importance of the trichomonad infection was attained by several veterinary practitioners in Switzerland and alpine regions of Germany who were confronted with problems of abortion and sterility in "Bang-free" cattle. When these men examined fresh genital exudate with reduced illumination under the low powers of the microscope they found the fluid teeming with *T. foetus.* This parasite had escaped detection by numerous experts in examinations of stained smears under oil immersion. Since 1925 the distribution of the genital trichomonad infection has been found world-wide and, as indicated in the monograph, has been the subject of many investigations.

The monograph, comprising 12 chapters, is an accurate, unbiased discussion of all available literature on the subject. The work might have been improved by more attention to the plan of its organization. For example, the chapter on "Morphology and Life Cycle" contains practically nothing concerning the life cycle of the parasite. This topic is discussed under "Transmission" in the chapter on "Symptoms and Lesions." It appears also that the data in the chapters on "Cultivation" and "Hydrogen-Ion Concentration" might well have been discussed in a chapter entitled "Physiology." As the volume stands, "Cultural Physiology" is discussed in a chapter entitled "Miscellaneous."

These criticisms do not detract markedly from the value of the monograph, and the present writer is in full accord with the following statement in the "Foreword" by Dr. W. L. Boyd: "Students of veterinary medicine, practitioners of veterinary medicine, and all others interested in developing a more healthful and therefore a more prosperous animal husbandry will find this contribution most helpful."

CHAS. W. REES

BOOKS RECEIVED

FENICHEL, DR. OTTO. *The Psychoanalytic Theory of Neurosis.* Pp. x + 703. W. W. Norton and Company, Inc. 1945.

BERGSON, HENRI. *The Creative Mind.* Pp. 9 + 307. Philosophical Library. 1946.

STIEGLITZ, DR. EDWARD J. *A Future for Preventive Medicine.* Pp. xvi + 77. The Commonwealth Fund. $1.00. 1945.